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THE PRESENT STATUS OF VIRUSES AND VIRUS DISEASES

EDWIN W. SCHULTZ, M.D.
Stanford University, Calif.

A hundred years ago the existence of viruses was unknown. The beginning of knowledge of this group of infectious agents indeed goes back only a half century. It is not yet fifty years since Beijerinck [1] established that the infectious agent of tobacco mosaic disease is filtrable and called it a "contagious living fluid" and since Loeffler and Frosch [2] identified the first ascertained virus disease of animals, foot-and-mouth disease. In the decade or so which followed a small number of other plant and animal diseases were identified as of virus origin. Among these were yellow fever, rabies, vaccinia-variola and poliomyelitis. But while the boundaries of knowledge regarding virus diseases widened gradually from this beginning, it was not until shortly after the first World War that the advances became rapid. This new period was ushered in by the discovery that bacteria, the outstanding partners of viruses in causing infections, are themselves victims of a virus disease. At first there was some uncertainty as to whether this disease, bacteriophagy or the Twort-d'Herelle phenomenon,[3] could be classified along with other then known virus diseases. It was viewed with caution by many. The precise nature of the agent responsible became the subject of warm debate, and one might ask today how much d'Herelle's staunch advocacy of bacteriophage as a living "ultramicrobe" had to do with the acceleration of interest in viruses which took root in the early twenties. Certainly bacteriophagy afforded an opportunity to study a virus disease under relatively simple and inexpensive conditions and still affords a favored approach to some of the unsolved problems in the virus field.[3f]

Whatever may be said regarding the stimulus which prompted the rapidly widening interest, the advances which have been made in knowledge of viruses during the past quarter of a century are little short of phenomenal. Many of these advances have been summarized in manuals, monographs and reviews.[4] No little of this advance can be credited to the professional pathologists, but a great deal must also be credited to men who set out to be chemists and physicists but later found themselves at the side of the animal and plant pathologists, dealing with aspects of problems which they alone were prepared to handle. Nowhere else in the advance of medical science was the need for cooperative effort greater, and nowhere else have the results proved more gratifying. What then have been the accomplishments of these years? What do men know with reasonable certainty about these agents, and what are some of the problems which remain unsolved? It is obvious to every one here, I know, that the achievements of a quarter of a century can scarcely be summed up in a quarter of an hour. I can recall only vaguely how I was led into this impossible task. There are, of course, moments far in advance of meetings when titles appear less ominous.

Men know today that virus infections are widespread. The invasion stretches from such lowly forms as bacteria to man. Many of the groups attacked by viruses are known to suffer with more than one virus disease. Bacteria are involved not by one but by many viruses—viruses which are distinguishable from each other in species or strain specificity, in size, in antigenic constitution and in other respects.[5] In other words, an impressive array of viruses attack bacteria alone. It is not known that there are viruses which attack protozoa, but to find that these forms also are included would not be surprising. In the plant kingdom many species of plants are known to be singled out by viruses of one kind or another,[5] and the studies which have been carried out in this area alone have advanced knowledge of viruses more than can be estimated. The

From the Department of Bacteriology and Experimental Pathology Stanford University School of Medicine.

Read in the Symposium on Virus Diseases before the Section on Pathology and Physiology at the Ninety-Sixth Annual Session of the American Medical Association Atlantic City, N. J., June 12, 1947.

1. Beijerinck, M. W.: Ueber ein Contagium vivum fluidum als Ursache der Fleckenkrankheit der Tabaksblätter, Verhandl. d. k. Akad. v. Wetensch. te Amsterdam (Sect. 2) **6**: 3-22, 1898; Centralbl. f. Bakt. (Abt. II) **5**: 27-33, 1899.

2. Loeffler and Frosch: Berichte der Kommission zur Erforschung der Maul- und Klauenseuche bei dem Institut für Infektionskrankheiten in Berlin, Centralbl. f. Bakt. (Abt. I) **23**: 371-391 (March) 1898.

3. (*a*) Twort, F. W.: An Investigation on the Nature of Ultramicroscopic Viruses, Lancet **2**: 1241-1243 (Dec. 4) 1915. (*b*) d'Herelle, F.: Sur un microbe invisible antagoniste des bacilles dysenteriques, Compt. rend. Acad. d. sc. **165**: 373-375 (Sept. 10) 1917; (*c*) The Bacteriophage and Its Behavior, English translation by G. H. Smith, Baltimore, Williams & Wilkins Company, 1926, p. 629. (*d*) Krueger, A. P.: The Nature of Bacteriophage and Its Mode of Action, Physiol. Rev. **16**: 129-172 (Jan.) 1936. (*e*) Delbrück, M.: Bacterial Viruses or Bacteriophages, Biol. Rev. **21**: 30-40 (Oct.) 1946. (*f*) Craigie, J.: The Significance and Applications of Bacteriophages in Bacteriological and Virus Research, Bact. Rev. **10**: 73-88 (Sept.-Dec.) 1946.

4. (*a*) Doerr, R., and Hallauer, C.: Handbuch der Virusforschung, ed. 1, Berlin, Julius Springer, 1938; ed. 2, 1939. (*b*) Gildemeister, E.; Haagen, E., and Waldmann, O.: Handbuch der Viruskrankheiten mit besonderer Berücksichtigung ehrer experimentellen Erforschung, Jena, Gustav Fischer, 1939, pp. 652 and 768. (*c*) Levaditi, C.; Lepine, P., and others: Les ultravirus des maladies humaines, Paris, Libraire Maloine, 1938, p. 1182. (*d*) Levaditi, C.; Lepine, P.; Verge, J., and others: Les ultravirus des maladies animales, ibid., 1943, p. 1126. (*e*) van Rooyen, C. E., and Rhodes, A. J.: Virus Diseases of Man, London, Oxford University Press, 1940. (*f*) Virus and Rickettsial Diseases with Especial Consideration of Their Public Health Significance, A Symposium Held at the Harvard School of Public Health, June 12-17, 1939, Cambridge, Mass., Harvard University Press, 1940, p. 907. (*g*) Members of the Rockefeller Institute for Medical Research: Virus Diseases, Ithaca, N. Y., Cornell University Press, 1943. (*h*) Lennette, E. W.: Recent Advances in Viruses: A Brief Survey of Recent Work on Viruses and Virus Diseases, Science **98**: 415-423 (Nov. 12) 1943. (*i*) Burnet, F. M.: Virus as Organism: Evolutionary and Ecological Aspects of Some Human Virus Diseases, Cambridge, Mass., Harvard University Press, 1945, p. 134. (*j*) Filtrable Virus Diseases, in Topley, W. W. C., and Wilson, G. S.: Principles of Bacteriology and Immunity, ed. 3, Baltimore, Williams & Wilkins Company, 1946, pp. 1869-1982.

5. (*a*) Holmes, F. O.: Handbook of Phytopathogenic Viruses, Minneapolis, Burgess Publishing Co., 1941, p. 221. (*b*) Bawden, F. C.: Plant Viruses and Virus Diseases, ed. 2, Waltham, Mass., Chronica Botanica Company, 1943, p. 294.

virus of tobacco mosaic disease was not only the first virus to be identified, but the first to be obtained in a purified form. This was the accomplishment of Wendell M. Stanley,[6] a chemist, who obtained the virus in a paracrystalline form in 1935, twelve years ago. This achievement marked the beginning of a new era in the study of viruses, one in which purification and more complete analysis of their individual properties became an important part of subsequent progress. For his achievement in virus chemistry Stanley was awarded the Nobel Prize last year.

In the animal kingdom the forms which are attacked range from insects to man. In many instances, the infections caused are strictly limited to one species or type of host, while in others the same viruses reach into quite unrelated hosts. In some cases the infections induced are apparently always associated with clinical manifestations; in others the infections are often apparent in one type of host and inapparent in another. The recognition that infections may occur in some hosts in a clinically inapparent form constitutes one of the important advances in the epidemiology of virus diseases. To know that a virus which attacks one type of host with devastating effect has or may have a silent reservoir in some other host is in itself a weapon against that virus. Inapparent infections are now known to be widespread. They have been recognized not only in animals but in higher plants and bacterial forms as well.[7]

There have been advances in the devices used for the study of viruses. The discovery of viruses may be credited to the use of bacteria-tight filters, such as are used to separate bacterial toxins from the organisms in a medium. It was Iwanowski's [8] apparent failure to catch the significance of his filtration results in the study of tobacco mosaic disease six years before Beijerinck made his observations which leaves him with a doubtful right to be regarded as the discoverer of filtrable viruses. At any rate, for a number of years virtually all that was known about viruses was that they passed bacterial filters. Nothing was known regarding their size, form and structure, and it is not surprising that Beijerinck in 1898 regarded the tobacco mosaic virus as something in true solution. The science of colloid chemistry was then still unborn. Investigators now have direct as well as indirect means of determining virus size and form. Collodion membranes gave the first information as to size—information which later proved more accurate than many had believed. This is a tribute to the colloid chemists who figured in this development, and particularly to Elford,[9] who provided the refinements necessary for dependable results. The next important development was the electron microscope.[10] It confirmed the fact that individual viruses differ widely not only in size (anywhere from 300 down to 10 microns) but in form and internal structure as well. It is now known that not all are spherical but that some are cuboidal or rectangular,[11] others rod shaped,[12] still others sperm shaped [13] and that certain ones are of highly irregular form.[14] The electron microscope has revealed that some viruses possess distinctive internal structure,[15] indicated in general by denser portions within their substance, and suggest a cellular type of organization.

Of equally great importance among the new tools of virus research are those which have been developed for the purification and physicochemical analysis of viruses. Although Stanley in 1935 first purified the tobacco mosaic virus by wholly chemical means, its purification was later more easily effected by differential ultracentrifugation,[16] which was made possible by the development of a new air turbine in a vacuum quantity centrifuge.[17] Out of this air driven quantity centrifuge evolved one of the current types of analytic centrifuges, with which it became possible to determine the homogeneity of supposedly purified virus suspensions, the molecular weight of a virus, its size or its density.[18] Other tools of modern chemistry and biophysics have also been pressed into use,[18c] and the sensitive methods of serology have been employed to reveal differences in their antigenic constitution.[19] Some of the advances and the remaining problems in this general area have recently been outlined by Wyckoff.[20]

Viruses are characterized in part by their dependence on living cells. None are able to grow in the absence of living cells, but this requirement has not prevented the cultivation of many of them apart from their hosts. This problem was met by drawing on the experiences of tissue culturists, and a number of viruses have now been cultivated in the presence of tissue explants. Some have been found to grow in the mere presence of living cells, free and unanchored in a suitable fluid medium,[21] but probably the greatest advance in the cultivation of viruses was the discovery by Goodpasture [22] that the developing egg can be effectively used to propagate them. This method as modified by Burnet [23] has now

6. Stanley, W. M.: Isolation of a Crystalline Protein Possessing the Properties of Tobacco-Mosaic Virus, Science **81**: 644-645 (June 28) 1935; Crystalline Tobacco-Mosaic Virus Protein, Am. J. Botan. **24**: 59-68 (Feb.) 1937.

7. Burnet, F. M.: Inapparent Virus Infections with Special Reference to Australian Examples, Brit. M. J. **1**: 99-103 (Jan. 18) 1936. Cowdry, E. V.: Inapparent Virus Diseases, Scient. Monthly **45**: 266-275 (Sept.) 1937. Craigie,[3f] Burnet,[4j] Holmes.[5a]

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10. Ruska, H.; von Borries, B., and Ruska, E.: Die Bedeutung der Uebermikroskopie für die Virusforschung, Arch. f. d. ges. Virusforsch. **1**: 155-169 (March) 1939. Marton, L.: The Electron Microscope: A New Tool for Bacteriological Research, J. Bact. **41**: 397-413 (March) 1941. Stanley, W. M.: Viruses and the Electron Microscope, Chron. Botan. **7**: 291-294, 1943. Mudd, S., and Anderson, T. F.: Pathogenic Bacteria, Rickettsias and Viruses as Shown by the Electron Microscope, J. A. M. A. **126**: 561-571 (Oct. 28); 632-639 (Nov. 4) 1944. Wyckoff, R. W. G.: Some Recent Developments in the Field of Electron Microscopy, Science **104**: 21-26 (July 12) 1946.

11. Green, R. H.; Anderson, T. F., and Smadel, J. E.: Morphological Structure of the Virus of Vaccinia, J. Exper. Med. **75**: 651-656 (June) 1942.

12. Stanley, W. M., and Anderson, T. F.: A Study of Purified Viruses with the Electron Microscope, J. Biol. Chem. **139**: 325-338 (May) 1941.

13. (*a*) Luria, S. E.; Delbrück, M., and Anderson, T. F.: Electron Microscope Studies on Bacterial Viruses, J. Bact. **46**: 57-76 (July) 1943. (*b*) Edwards, O. F., and Wyckoff, R. W. G.: Electron Micrographs of Bacterial Cultures Infected with Bacteriophage, Proc. Soc. Exper. Biol. & Med. **64**: 16-19 (Jan.) 1947.

14. Bang, F. B.: Filamentous Forms of Newcastle Virus, Proc. Soc. Exper. Biol. & Med. **63**: 5-7 (Oct.) 1946. Cunha, R.; Weil, M. L., and others: Purification and Characters of the Newcastle Disease Virus (California Strain), J. Immunol. **55**: 69-89 (Jan.) 1947.

15. d'Herelle,[3j] Green, Anderson and Smadel,[11] Luria, Delbruck and Anderson.[13a]

16. Wyckoff, R. W. G., and Corey, R. B.: The Ultracentrifugal Crystallization of Tobacco Mosaic Virus Protein, Science **84**: 513 (Dec. 4) 1936.

17. Bauer, J. H., and Pickels, E. G.: A High Speed Vacuum Centrifuge Suitable for the Study of Filtrable Viruses, J. Exper. Med. **64**: 503-528 (Oct.) 1936. Svedberg, T., and Pedersen, K. O.: The Ultracentrifuge, Oxford, Clarendon Press, 1940, p. 478.

18. (*a*) Bauer, J. H., and Pickels, E. G.: An Improved Air-Driven Type of Ultracentrifuge for Molecular Sedimentation, J. Exper. Med. **65**: 365-586 (April) 1937. (*b*) Pickels, E. G.: The Ultracentrifuge: Practical Aspects of the Ultracentrifugal Analysis of Proteins, Chem. Rev. **30**: 341-355 (June) 1942. (*c*) Lauffer, M. A.: Virus Studies: Biophysical Methods, in Glasser, O.: Medical Physics, Chicago, The Year Book Publishers, Inc., 1944, p. 1653.

19. Smadel, J. E., and Shedlovsky, T.: Antigens of Vaccinia, Ann. New York Acad. Sc. **43**: 35-46 (April) 1942. Rivers, T. M.: Virus Diseases with Particular Reference to Vaccinia, in Virus Diseases,[4g] p. 3.

20. Wyckoff, R. W. G.: Some Biophysical Problems of Viruses, Science **101**: 129-136 (Feb. 9) 1945.

21. Sanders, M.: Cultivation of the Viruses: A Critical Review, Arch. Path. **28**: 541-586 (Oct.) 1939.

22. Goodpasture, E. W.; Woodruff, A. M., and Buddingh, G. J.: The Cultivation of Vaccine and Other Viruses on the Chorioallantoic Membrane of Chick Embryos, Science **74**: 371-372 (Oct. 9) 1931.

23. Burnet, F. M.: A Virus Disease of the Canary of the Fowl-Pox Group, J. Path. & Bact. **37**: 107-122 (July) 1933.

been successfully applied to a considerable number of viruses. It has found application in the production of viruses for use as vaccines, in the titration of viruses (in which it substitutes for animals), in serologic studies and in the diagnosis of some virus diseases.[24]

A striking feature of viruses is their heterogeneity when considered as a group. They frequently exhibit marked differences in the degrees to which they resist certain physical and chemical agents. Extensive studies have made it clear that they are "individualists" and that generalizations from observations on any one of them are apt to rest insecurely. They are not alike in their resistance to heat, cold, drying, hydrogen ion concentrations, organic or inorganic chemical compounds, or to the action of individual enzymes.[25] They are not alike in their chemical constitution or in their biochemical properties.[26] There are resemblances, as well as differences, of course, but taken as a whole they are quite as heterogeneous in makeup and properties as the various hosts they prey on.

They differ in their individual tropisms; that is, in the particular types of cells which they single out for invasion and subsequent multiplication. This usually means some kind or kinds of cells within some particular host. This tropism is apt to be a fairly constant property of a given virus. Observers have become aware, however, that the tropism of a virus may be much less restricted and less fixed than they are sometimes led to believe and that it is also subject to variation.[27] This variation may depend on only slight tissue or environmental differences. The conversion of street rabies virus into fixed virus by brain to brain passage is associated with a loss of ability of the virus to implant itself in peripheral nerves. The variation may reach to new cells or tissues, sometimes with complete loss of the initial tropism. It may occur independently of variation in the antigenic constitution of a virus.

What determines the tropism of a virus is something about which little is known. There is some evidence from observations on bacteriophagy that the antigenic constitution of the host cell and susceptibility to a given virus are related.[28] Since antigenic constitution may be largely determined by genetic factors, it may not be possible to do much artificially to alter these natural relationships. This is an area in which further work is needed.

Variations are also exhibited by viruses in other respects,[29] including variation of their antigenic constitution. The latter may be associated with variation of tropism or may occur independently of it. Variation of antigenic constitution has an important bearing on the serologic identification of viruses. Investigators have learned that viruses which cause individual diseases may fall into different serologic groups and that variation may result from new environmental conditions which are imposed on the virus. Such variations fortunately do not as a rule occur with great ease, so that it has been possible to base much of what is known today about differences among viruses on serologic observations.

Viruses differ in their individual proliferative powers. There are low and high titer viruses. These differences relate not only to viruses causing different diseases but also to individual strains of a given virus. They may not be the same for a given strain when it is propagated in another host, but they tend to become stabilized for a given host and frequently remain the same for it in spite of many serial passages. Little is known regarding the factors which determine these individual differences. They appear to be represented in both the host and the parasite. Low titer strains may not lack in invasiveness and, like more virulent strains, may become widely disseminated in the tissues of the respective hosts, but they seem to lack the ability to multiply sufficiently within the cells they invade to damage them seriously. Such strains may be partly responsible for subclinical infections and naturally acquired active immunity to individual virus diseases.

Little is known about how viruses act to produce their harmful effects on the cells they invade, since they are not as a whole identified with toxic properties. More information is needed in this area.

Since viruses exhibit cell tropisms, the lesions induced center around individual kinds of cells. The effects produced on these cells can and do differ widely. Considering viruses as a whole, these effects range from rapid cell death to mere stimulation of cell growth and multiplication, the latter being a characteristic of the tumor group.[30] To state the effects so broadly is to oversimplify the story somewhat.[31] The distinctive lesion is at any rate an involvement of some kind of cell. Whatever inflammatory reaction may be present is there as a secondary response to this cell injury.

Viruses differ also with regard to the production of inclusion bodies. Some give rise to them; others do not. Those which do, may produce them either in the cytoplasm of the cell or in the nucleus. The cytoplasmic inclusions produced by some viruses consist largely of aggregations of virus particles; those produced by certain other viruses (rabies) seem to consist chiefly of retrograde products derived from the cell itself. In certain virus diseases of plants (tobacco mosaic disease) amorphous cytoplasmic inclusions have been observed to give rise to crystalline inclusions consisting of "virus protein."[32] Nuclear inclusions also differ, the more indicative of a virus infection being the type A inclusions described by Cowdry.[33] Cell inclusions of certain types may be formed in the apparent absence of virus infections, and these "nonspecific inclusions" must, of

24. Beveridge, W. I. B., and Burnet, F. M.: The Cultivation of Viruses and Rickettsiae in the Chick Embryo, Medical Research Council, Special Report Series, no. 256, London, His Majesty's Stationery Office, 1946, p. 92.

25. Stanley, W. M.: Biochemistry and Biophysics of Viruses: I. Inactivation of Viruses by Different Agents, in Doerr and Hallauer,[48] p. 447.

26. Stanley, W. M.: The Architecture of Viruses, Physiol. Rev. **19**: 524-556 (Oct.) 1939; The Biochemistry of Viruses, in Annual Review of Biochemistry, Stanford University, Calif., Stanford University Press, 1940, vol. 9, p. 545; Chemical Properties of Viruses, Scient. Monthly **53**: 197-210 (Sept.) 1941. Bryan, W. R., and Beard, J. W.: Studies on the Purification and Properties of the Rabbit-Papilloma-Virus Protein, J. Nat. Cancer Inst. **1**: 607-673 (April) 1941. Loring, H. S., and Schwerdt, C. E.: Studies on the Purification of Poliomyelitis Virus, J. Exper. Med. **75**: 395-406 (April) 1942. Taylor, A. R.; Sharp, D. G.; Beard, D., and Beard, J. W.: Isolation and Properties of Equine Encephalomyelitis Virus (Eastern Strain), J. Infect. Dis. **72**: 31-41 (Jan.-Feb.) 1943. Glaser, R. W., and Stanley, W. M.: Biochemical Studies on the Virus and the Inclusion Bodies of Silkworm Jaundice, J. Exper. Med. **77**: 451-466 (May) 1943. Bourdillon, J.: Purification, Sedimentation and Serological Reactions of the Murine Strain of SK Poliomyelitis Virus, Arch. Biochem. **3**: 285-297 (Feb.) 1944. Duffy, C. F., and Stanley, W. M.: Studies on the Biochemical, Biophysical, and Immunogenic Properties of Japanese B Type Encephalitis Virus and Vaccines, J. Exper. Med. **82**: 385-410 (Dec.) 1945. Knight, C. A.: The Preparation of Highly Purified PR8 Influenza Virus from Infected Mouse Lungs, ibid. **83**: 11-24 (Jan.) 1946.

27. Doerr, R.: Die Tropismen und specifischen Lokalisationen der Virusarten, in Doerr and Hallauer,[48] p. 826.

28. The Factors That Determine Phage Specificity, in Topley, W. W. C., and Wilson, G. S.: Principles of Bacteriology and Immunology, Baltimore, Williams & Wilkins Company, 1946, p. 338.

29. Findalay, G. M.: Variation in Viruses, in Doerr and Hallauer,[48] p. 861.

30. Rous, P.: Viruses and Tumors, in Virus Diseases,[42] p. 147.

31. Rivers, T. M.: Pathology of Virus Diseases, in Lane Medical Lectures: Viruses and Virus Diseases, Stanford University, Calif., Stanford University Press, 1939, p. 33.

32. Findlay, G. M.: Inclusion Bodies and Their Relationship to Viruses, in Doerr and Hallauer,[48] p. 292.

33. Cowdry, E. V.: The Problem of Intranuclear Inclusions in Virus Diseases, Arch. Path. **18**: 527-542 (Oct.) 1934.

course, be differentiated from those which are specific.[32] Any formation of inclusion bodies must require time. They are therefore not expected in cells which succumb quickly to the impact of a virus. They are, on the other hand, not necessarily produced in cells which resist the action of a virus. They are helpful when present and characteristic, but their absence does not exclude the possible presence of a virus infection.

Clinically, virus diseases are about as varied as any other group of infectious diseases. There is nothing especially distinctive about many of them. While some can easily be diagnosed clinically, others definitely require laboratory help. This is particularly true of the neurotropic virus diseases, which often cannot be differentiated without such aid. Some virus infections seem to occur regularly in a clinically evident form; others may occur in a subclinical as well as a clinically apparent form in the same type of host, and still others, in an apparent form in one type of host and an inapparent one in another. It is obvious that the existence of mild or inapparent infections cannot be recognized without laboratory help.

The laboratory procedures that aid in the diagnosis of virus diseases have advanced considerably over those of even a decade ago. They are, however, for the most part highly specialized and not of the kind which can usually be rendered by the ordinary clinical laboratory. Special facilities and a suitably trained personnel are required. The procedures are varied but in general consist either of attempts to effect a direct isolation and identification of the virus or of tests that reveal whether or not viral antibodies are in the patient's blood.[34] The latter may mean tests for virus-neutralizing antibodies or wholly in vitro tests for complement-fixing or agglutinating antibodies. The first-named type is based on inactivation of virus and is therefore partly an in vivo test carried out with susceptible experimental hosts. Wholly in vitro tests, such as the complement fixation test, are much more convenient and less costly than neutralization tests, but unfortunately they are not as uniformly applicable to the diagnosis of virus diseases. A certain minimum amount of virus material must be present in the antigen that is used in such a test, and this is something not easily realized with materials representing all kinds of virus infections. However, the complement fixation test, which is the more sensitive of the two in vitro tests named, has proved its value in the diagnosis of several virus diseases.[35] Even with the more generally serviceable neutralization test it is important to bear in mind that antibodies often do not make their appearance in the patient's blood until late in the disease or after recovery. A large part of the value of these tests therefore lies in the identification of the cause of a past infection rather than that of a current illness. In any case it is important to procure a specimen of serum early during the course of a patient's illness, for comparison with later specimens.[34b]

One of the largely unsolved problems in regard to virus diseases is that of specific therapy. Any sort of direct attack is complicated by the fact that viruses are intracellular infectious agents, also by the fact that the initial invasion is likely to be widespread and to involve many susceptible cells simultaneously. Once a virus particle has found its abode within a cell, it is apparently out of the reach of potential therapeutic agents which may thereafter be brought to the environment of the cell. Unlike intercellular bacterial parasites, it is no longer exposed to whatever may be successfully conveyed to the area by the blood. Antibody molecules are too large to follow the virus into the cell, and chemical agents which might conceivably do so and there inhibit or destroy it, would seem likely to injure the cell also. The problem is therefore a difficult one. However, in spite of the theoretic difficulties presented by this intracellular relationship, hopeful chemotherapeutic results have recently been reported, following the administration of sulfonamide compounds and of penicillin, in certain individual virus and rickettsial infections, suggesting that such a direct approach may not be entirely out of the question.[36] The solution of this problem may have to be sought, however, in the form not of direct but of indirect measures—measures which may serve to make the protoplasm of the cell less suitable for the multiplication of the entrenched virus or less vulnerable to its effects. It is possible, of course, that the factors which determine the character of the protoplasmic soil and its susceptibility to a given virus are largely genetic in nature and to this extent out of artificial control, but whatever may be possible by such indirect means would seem to be in greater harmony with the normal physiology of a cell than any attempt to attack the virus directly.

Much of the control maintained over virus diseases is rooted in their immunity relationships. Because individual viruses are more or less highly dependent on suitable cell pabula, differences of the protoplasmic soil, or natural immunity, constitute one of the limiting factors. Virus infections, when they occur, moreover, are characterized by the solidity and the durability of the immunity which they leave in their wake, there being few exceptions to this rule. The immunities which follow natural infections are commonly associated with antibodies that appear in the blood. It is generally held, however, that the initial stimulus leading to their formation is not wholly responsible for the durable immunity and that this would probably not last nearly as long were it not for the fact that, following many and possibly most virus diseases, some virus persists in the recovered host and serves to keep the immunity alive.[37] This thought—that there is persistence of virus after recovery—impresses one at first as an incongruity, but the matter clears up when one recalls that viruses are ordinarily intracellular and that antibody molecules cannot reach into cells. In addition to the role played by antibodies, there may be changes induced in the protoplasm of the naturally susceptible cells (acquired tissue immunity). The evidence for this consists of the acquired resistance following certain virus infections which have been demonstrated in the absence of antibodies, either before these had an opportunity to appear, or in types of infection in which antibodies seldom are found in the blood after recovery; also, observations have been recorded showing that a high antibody level is not always associated with a high degree of resistance.[37]

34. (*a*) Sulkin, S. E., and Harford, C. G.: The Laboratory Diagnosis of Virus Diseases, J. A. M. A. **122**: 643-648 (July 3) 1943. (*b*) Rivers, T. M.: Virus Diseases of the Nervous System, ibid. **132**: 427-430 (Oct. 26) 1946.

35. Henle, W.; Henle, G.; Vincent, G., and Chambers, L. A.: Studies on Complement Fixation with the Viruses of Influenza, J. Immunol. **48**: 163-180 (March) 1944. Dulaney, A. D., and Packer, H.: Observations Upon the Specificity of the Complement-Fixation Test for Lymphogranuloma Venereum, ibid. **55**: 53-60 (Jan.) 1947. Perlowagora, A., and Hughes, T. B.: The Complement Fixation Test in Yellow Fever Epidemiology: The Use of Globulins in Immunity Surveys, ibid. **55**: 103-119 (Feb.) 1947. DeBoer, C. J., and Cox, H. R.: Specific Complement-Fixing Diagnostic Antigens for Neurotropic Virus Diseases, ibid. **55**: 193-204 (Feb.) 1947. Sulkin and Harford.[34a] Rivers.[34b]

36. Mudd, S.: Can Chemotherapy Be Extended to Include the Intracellular Disease Agents? J. Bact. **49**: 527-537 (July) 1945.

37. Rivers, T. M.: Immunological and Serological Phenomena of Virus Diseases, in Lane Medical Lectures: Viruses and Virus Diseases, Stanford University, Calif., Stanford University Press, 1939, p. 53.

Effective immunization seems to require the use of active virus, but strains safe enough to be used as vaccines are few. Vaccinia virus, fixed rabies virus and strain 17D yellow fever virus are three outstanding examples. But while there are few such vaccines available, it has proved possible to establish immunities of short duration against some virus diseases by the use of suspensions of inactivated viruses. Influenza and equine encephalomyelitis are among the diseases which have recently been brought into this fold. This use of inactivated viruses cannot do more than set up a certain level of antibody formation, and since the response tends to die down in the absence of a persistent stimulus, such as may result from a previous infection or may be induced by inoculation of active virus, the immunizations require repetition, possibly at intervals of six months to a year, to maintain their effectiveness.

Regarding passive immunity, it is well recognized that such antibodies as a prospective mother may happen to possess for given viruses are frequently transferred to the fetus and that they may convey to it a degree of protection which will endure for some months after its birth. Passive immunity can also be induced artificially against certain virus diseases. Indeed, it is preceding exposures to viruses that antiserums serve their greatest usefulness, for once a virus particle has found the interior of a cell it is out of reach and remains so unless its house falls. While immune serums have prophylactic value, their prophylactic use has been limited, one of the reasons being that it is often difficult to say whether immune serum is required or not. The patient may already be immune. There are virtually no simple tests for determining this. Recently evidence has been obtained that cutaneous allergy accompanies naturally acquired active immunity in cases of mumps,[38] apparently in the same way that allergy follows successful smallpox vaccination, but sufficient observations have been made on other virus diseases to indicate that cutaneous allergy is not always easily demonstrable after recovery. It is clear, of course, that whenever immune serum is used prophylactically, even in amounts which will prevent infection entirely, it will probably leave the recipient fully susceptible again after the passive protection has worn off. In the use of human measles immune serum, for example, the objective is to abort the infection but not to prevent it entirely.

Much of the control that is now exercised over virus diseases rests on the epidemiology [39] of these diseases. Much information has been gathered in these years, but much more is needed to enable physicians to deal with certain virus diseases, such as poliomyelitis. It is known that some are commonly spread by direct or indirect contact, and that some are transmitted by insects. The role of the latter in the virus diseases of animals and plants has been the subject of extensive investigations over a number of years and has assumed increasing importance with the recognition that vast silent reservoirs of inapparent infections may sometimes exist in hosts quite unrelated to the ones in which clinical manifestations are more common—reservoirs from which insect vectors can carry the infection to more susceptible hosts. The detection of these reservoirs investigators usually owe first to serologic observations made on potential hosts and later to successful attempts to isolate the virus from them. With improvements of serologic methods, such as the wider and more effective use of the complement fixation test, these reservoirs will become easier to identify.

I have merely touched here and there on the present state of knowledge of viruses. It was not possible to do more. One may be sure, however, that the science of virology has reached maturity and that it will be equal to the problems which remain.

39. Gordon, J. E.: Epidemiological Problems of Virus Diseases, in Virus and Rickettsial Diseases,[4f] p. 3.

38. Enders, J. F.; Cohen, S., and Kane, L. W.: Immunity in Mumps: II. Development of Complement-Fixing Antibody and Dermal Hypersensitivity in Human Beings Following Mumps, J. Exper. Med. **81**: 119-135 (Jan.) 1945.

THE PRACTITIONER AND THE VIRUS DIAGNOSTIC LABORATORY

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Great advances have been made in the diagnosis, the control and the treatment of viral and rickettsial diseases in the last few years. They have resulted from intensive research carried out by laboratory workers, with the patient assistance of the practicing physician. The latter has been putting his time and effort into a long term investment which has now begun to pay dividends. My main object here is to advise him how to use his dividends wisely and how to avoid spending the principal unwittingly. I shall point out those methods which are now sufficiently well developed and standardized to be employed as routine diagnostic procedures. These every physician has a right to expect will be made available to him. In addition, I shall mention those procedures which are still so highly specialized that competent research workers are required for their satisfactory accomplishment. These research procedures are not the physician's to demand for use in routine diagnostic work. Rather they are the physician's to request only, and then in an investigation in which he cooperates with the laboratory worker. If the physician fails to employ these research procedures wisely, he is wasting the common investment in the advancement of medicine.

The isolation and the identification of viral and rickettsial agents are still research procedures. Let the physician recognize them as such and refrain from requesting them unless he is willing and able to cooperate in the investigation. In only a few instances will the isolation of the agents infectious for man provide useful information which could not have been obtained more quickly, easily and cheaply by serologic methods. It is not my purpose to present the technical details of laboratory procedures; for these, clinicians may consult their own laboratory specialists. I shall merely say that the recovery of a transmissible agent by inoculating animals with material suspected of containing it is difficult; furthermore, this is only the first step. The next step, identification of the agent, usually requires an elaborate organization and considerable time. At the Army Medical Department Research and Graduate School, which is completely equipped for such work, we consider ourselves fortunate if we are able to isolate and identify variola virus in three days and rabies virus in eight. There are more direct methods which will establish the diagnosis in less time. A minimum of ten days to three weeks is required, even under optimal conditions, for isolation and identification of such common viruses as those of lymphocytic choriomeningitis, influenza, psittacosis, St. Louis encephalitis and West-

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From the Department of Virus and Rickettsial Diseases, Army Medical Department Research and Graduate School, Army Medical Center.

ern and Eastern equine encephalitis, and of the Rickettsia of epidemic and murine typhus, spotted fever and rickettsialpox.

Such rapid identification of viral and rickettsial agents requires complete facilities for performing various serologic and cross immunity tests, and these in turn require the constant maintenance of a museum of infectious agents, as well as stocks of known antigens, antiserums and immune animals. In incompletely equipped laboratories the identification of a newly isolated virus awaits the acquisition of such materials, which must be prepared locally or procured from another laboratory. Before I leave the subject of isolation, let me reiterate that the advancement of knowledge requires that this method be used in order that new agents may be discovered, but it is not necessary for the diagnosis of most of the viral and rickettsial diseases of man, for which adequate serologic procedures have been developed. If isolation studies seem to be indicated, the clinician should consult his virus specialist as to the type of material which is to be obtained and how such material is to be shipped.

Serologic Tests for the Diagnosis of Common Viral and Rickettsial Diseases of Man in North America

	Type of Test and Time for Collecting Specimens					
	Complement Fixation, Day of Bleeding		Neutralization, Day of Bleeding		Miscellaneous Agglutination, Day of Bleeding	
Group and Disease	Early *	Late †	Early *	Late †	Early *	Late †
					(R.B.C. Agglutination Inhibition)	
Respiratory group						
Influenza A and B	..	..	..	..	2	8
					(Cold Hemagglutinins)	
Atypical pneumonia	..	..	..	..	7	21
Psittacosis-lymphogranuloma venereum	10	21				
Rickettsial group					(Weil-Felix)	
Typhus: murine	10	21	..	..	6	12
Typhus: epidemic	10	21	..	..	6	12
Spotted fever	10	21	..		6	12
Q fever	10	21				
Rickettsialpox	10	21				
Aseptic meningitis						
Lymphocytic choriomeningitis	10	21				
Mumps meningitis	6	21				
American epidemic encephalitides						
St. Louis	..	..	8	21		
Western equine	..	..	6	21		
Eastern equine	..	..	6	21		

* The day given is the last that can be expected to antedate the first appearance of antibody or any sharp rise of antibody titer.

† The day given is the first day on which an appreciable amount or the maximum level of antibody may be expected to be present.

There are satisfactory diagnostic serologic tests for a number of the viral and rickettsial diseases occurring in the United States, and they should be available to all physicians. The tests are listed in the table. The materials of a few of these are not difficult to prepare; however, most of the diagnostic antigens require special facilities for their manufacture, but, once prepared, they are stable and noninfectious. The complement-fixing and the agglutinating antigens required for the tests listed in the table are prepared at the Army Medical Department Research and Graduate School, and a number of them are supplied to Army laboratories throughout the world. Unfortunately, in some respects we are authorized to serve military personnel only and cannot furnish the materials to nonmilitary laboratories. It is my firm conviction that these diagnostic antigens will be made generally available within a few years, for several commercial biologic houses have evinced an interest in the manufacture of such antigens. Their efforts should be encouraged, since the wide application of these diagnostic tests must await a ready supply of the antigens.

If one may assume that noninfectious viral and rickettsial antigens can be supplied freely, then all of the diagnostic procedures listed, except the neutralization tests for the encephalitides, could be performed in any hospital laboratory in which satisfactory Wassermann tests and bacterial agglutination tests are done. I know of no laboratories other than those of the Army Medical Department School and of the National Institute of Health which regularly perform all or even the majority of the tests listed. Several of the state and municipal laboratories provide some of the diagnostic procedures, and a number of laboratories associated with teaching institutions routinely perform a few of the tests. The delay in making these methods available to physicians is dependent on the nonavailability of the antigens.

It is not too difficult for a good hospital laboratory to run a few neutralization tests, but some special equipment and training are necessary. Neutralization tests are designed to detect protective antibodies and are performed by mixing the patient's serum with diluted virus and injecting the mixture into a susceptible animal. If obvious disease develops, this indicates that the serum contains no protective substances, while if the animal remains well, the serum does possess neutralizing antibody. Neutralization tests can be relatively simple and give useful diagnostic data. Virus workers harangue about the advantages of certain modifications of the technic, but most of their arguments belong in the category of the theologic question of how many angels can stand on the point of a needle.

The neutralization technic is listed in the table for the diagnosis of only three diseases, viz., the epidemic encephalitides of North America. These infections occur only in the summer and have a limited geographic distribution. Therefore, a laboratory serving a given area would be required to do only certain of these tests and then for only part of the year. Those situated along the Atlantic seaboard and the eastern coast of the Gulf of Mexico should make routine diagnostic tests for Eastern equine encephalitis but not for Western equine encephalitis or St. Louis encephalitis. Laboratories in the area bounded roughly by the Mississippi River, the Pacific coast and the Canadian and Mexican borders should perform tests for St. Louis encephalitis and Western equine encephalitis but not for Eastern equine encephalitis. There is one area, however, where all three should be done, namely, eastern Texas, Louisiana and Mississippi, for in this section all three agents are known to occur.

The serologic methods mentioned in the table represent only a portion of those which have been employed for diagnostic work. Thus, some modification of the Hirst agglutination inhibition test is used almost exclusively in the diagnosis of influenza, but neutralization and complement fixation technics were employed satisfactorily until the simpler Hirst method became available. In the diagnosis of lymphocytic choriomeningitis the neutralization test is extremely useful, while in diagnostic studies of St. Louis and Western equine encephalitis complement fixation technics have been

employed. In the diagnosis of rickettsial diseases the results obtained with rickettsial agglutination tests are as valuable as those derived from complement fixation. The technics listed in the table have been selected for clinical use because they can supply the greatest amount of useful data with the smallest expenditure of money, equipment and personnel.

The various methods employed in the diagnosis of viral and rickettsial diseases were described in detail at a recent symposium, and the descriptions will soon be published in book form;[1] this material should be consulted for details and references.

The discussion so far has centered around those things which physicians may and should ask the laboratory man to do to assist them in their practice. Now I should like to devote a little time to the things they should do in order to obtain usable information from the diagnostic tests which they request. The physician should always aim to collect serum specimens in such a manner that a rise in antibody titer can be demonstrated during convalescence. He should always get at least two samples of serum from every patient suspected of having a diagnosable viral or rickettsial disease. The detection of specific antibodies is generally worthless if a single specimen of serum is examined in a neutralization test for encephalitis, a Hirst test for influenza or a complement fixation test for the psittacosis-lymphogranuloma group, or for mumps. The serums of too many persons contain these antibodies as a result of previous infections which may or may not have been recognized. Antibodies appear more quickly in some instances than in others. The early serum should be drawn before antibody has appeared or before a sharp rise of titer has occurred. The last day on which these conditions are met is given in the column in the table titled "Day of Bleeding—Early." The earliest day on which antibody can be expected to appear in appreciable amounts or to reach its maximal level is given in the column "Day of Bleeding—Late." It is not enough that the physician take the specimens at the proper times; he must also pass on this information to the laboratory man so that the latter can examine the material intelligently.

SUMMARY

Practical methods are now available for the diagnosis of many of the viral and rickettsial diseases which physicians encounter. These methods are not now generally available but will be as soon as the necessary special antigens can be supplied. The commercial manufacture of the antigens is the next step, which must be accomplished before these technics may be used extensively for the diagnosis of disease.

1. Report of Committee on Diagnostic Procedures in Virus and Rickettsial Diseases, New York, American Public Health Association, 1948, to be published.

Rheumatism.—That rheumatoid arthritis may at times be a psychosomatic disease has been suggested, but most authorities agree that psychic disturbances alone cannot cause the disease. Grief, worry or anxiety may occasionally act as precipitating agents and in some cases appear to be temporally related to fluctuations in the clinical course of rheumatoid arthritis. But while emotional upsets may act as trigger mechanisms to set off the disease process, it is probable that the body must first harbor the causative factor (infectious agent or whatever the factor is).—Boland, E. W.: *California Medicine*, April 1948

ELECTRON MICROSCOPIC STUDY OF VIRUSES

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Electron microscopes make it possible to see the elementary infectious particles of the smallest viruses and thus to study these hitherto invisible agents of disease in the same general way that bacteria have been studied with optical microscopes. In such a study the first problem that arises, and one that must be successfully met before others can properly be attacked, involves learning to recognize the individual units of virus activity among the masses of tissue and other extraneous material with which they are associated. For this a virus should be available in purified form; otherwise, it is as dangerous to ascribe virus activity to specific objects seen in the microscope as it is to pick some particular organism in a mixed bacterial culture as being responsible for a disease induced by the culture as a whole. Viruses grow only on living matter, and they must therefore usually be separated from the large masses of host cells that have nurtured them. Research directed toward finding ways to do this will continue to be essential to a developing morphology of viruses.

Electron microscopy of purified suspensions has already provided accurate descriptions of the elementary particles of a number of viruses of plants and animals. Some have characteristic appearances that allow them to be recognized in crude infected tissue. Others, differing little in shape from normal constituents of healthy cells, may always remain hard to recognize in infected material.

The largest viruses have distinctive shapes. Some, like the poxes,[1] are bricklike. The psittacine viruses—psittacosis, lymphogranuloma, feline pneumonitis and other members of this group—are less uniform in appearance.[2] Separate elementary bodies appear as collapsed spheres, but there are also present objects containing several spheres similar to the free bodies. Some bacteriophages are spermlike,[3] with heads that show characteristic internal structures and tails the appearance of which depends on the strain (fig. 1). Virus particles of the Newcastle disease of chickens are said[4] sometimes to have sheathlike appendages and sometimes to be without them. All the very small viruses of animals and most of the viruses of plants thus far photographed have spherical or nearly spherical particles. The virus[5] of rabbit papilloma and the less stable viruses of Eastern and Western encephalomyelitis[6] are of this sort. The virus of poliomyelitis also

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From the National Institute of Health.

1. (*a*) Green, R. H.; Anderson, T. F., and Smadel, J. E.: J. Exper. Med. **75**: 651, 1942. (*b*) Sharp, D. G.; Taylor, A. R.; Hook, A. E., and Beard, J. W.: Proc. Soc. Exper. Biol. & Med. **61**: 259, 1946. (*c*) Groupe, V.; Oskay, J., and Rake, G.: ibid. **63**: 477, 1946.

2. Rake, G.; Rake, H.; Hamre, D., and Groupe, V.: Proc. Soc. Exper. Biol. & Med. **63**: 489, 1946. Davis, D. J., and Wyckoff, R. W. G.: Unpublished data.

3. Luria, S. E.; Delbrück, M., and Anderson, T. F.: J. Bact. **46**: 57, 1943. Edwards, O. F., and Wyckoff, R. W. G.: Proc. Soc. Exper. Biol. & Med. **64**: 16, 1947. Sharp, Taylor, Hook and Beard.[1b]

4. Bang, F. B.: Proc. Soc. Exper. Biol. & Med. **63**: 5, 1946; **64**: 135, 1947.

5. Sharp, D. G.; Taylor, A. R.; Beard, D., and Beard, J. W.: Proc. Soc. Exper. Biol. & Med. **50**: 205, 1942. Sharp, Taylor, Hook and Beard.[1b]

6. Sharp, D. G.; Taylor, A. R.; Beard, D., and Beard, J. W.: Morphology of Eastern and Western Strains of Virus of Equine Encephalomyelitis, Arch. Path. **36**: 167 (Aug.) 1943.

has been reported[7] to be spherical as seen in purified extracts of diseased cord tissue.

The particles of many viruses of animals are not uniform in size; instead their diameters seem to be distributed, often widely, about a mean value. This variation in size is clearly evident in the influenza spheres[8] of figure 2. The elementary particles of all

Fig. 1.—Strain T[4] bacteriophage particles among colon bacilli on the surface of an agar culture undergoing lysis. A collodion replica, chromium shadowed.

purified viruses of plants, on the other hand, show the sort of dimensional uniformity to be expected of chemical molecules. Thus the spherical particles of the bushy stunt virus[9] have diameters that are the same within the limit of measurement (fig. 3). Rods of the tobacco mosaic virus,[10] though often of different lengths in purified preparations, have a uniform diameter.

No virus of animals has yet been crystallized, and it is hard to imagine how particles of varying size could arrange themselves into the three-dimensionally regular patterns that characterize a true crystal. Some viruses of plants, on the other hand, can easily be crystallized, and this is undoubtedly a consequence of the uniformity of their particles. Particles of uniform cross section but different lengths can pack with regularity in two but not in three dimensions. The tobacco mosaic virus forms such paracrystalline aggregates.[11] Plant viruses having spherical particles, on the other hand, form crystals in which their elementary bodies are as well arranged as are the molecules of other crystalline proteins. In favorable instances, the electron microscope reveals the exact details of this regularity[12] and thus provides a new and most direct method of determining crystal structure. Studies of these arrangements are already giving a precise insight into the basic phenomena of crystallization.

Once the morphologic characteristics of a virus are sufficiently understood, this understanding can serve as a basis for studying other of its important characteristics. Thus one can investigate by direct observation the products of reactions in which it takes part. The immune reaction that occurs between a virus and its specific antibody is undoubtedly one of the most important of these. Since individual molecules as small as those of the serum proteins can now be photographed, it has become feasible to examine this reaction down to its ultimate molecular level. This requires an antigen

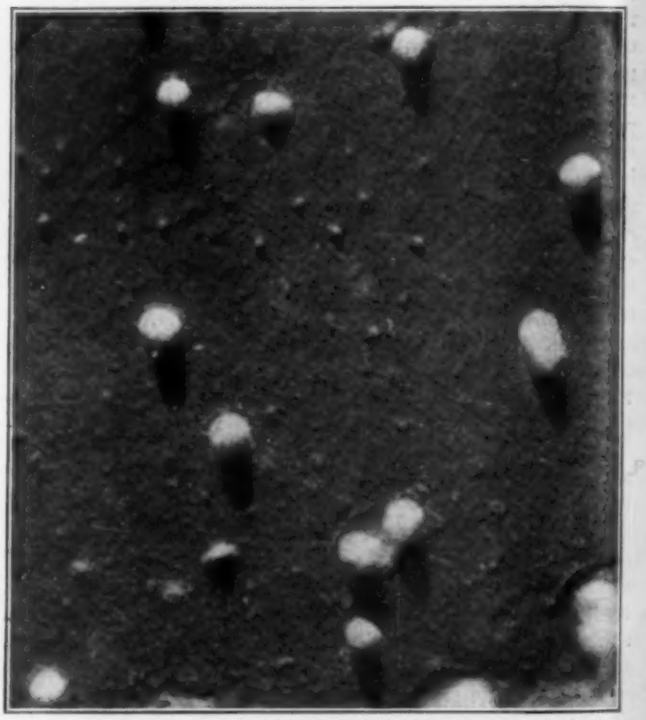

Fig. 2.—Elementary bodies in an ultracentrifugally purified suspension of type A influenza virus cultured in chick embryos. Chromium shadowed; magnification, 58,000.

comparable in size with the antibody molecules; the smallest viruses approach this requirement. On the electron microscopic scale, the most striking evidence that a reaction occurs between a plant virus, for example, and its immune serum is the microagglutination[13] in which not more than a score of virus particles may be present in a single floc (fig. 4). The ability to observe a reaction involving such a fantastically small amount

7. Loring, H. S.; Marton, L., and Schwerdt, C. E.: Proc. Soc. Exper. Biol. & Med. **62**: 291, 1946. Loring, H. S.: ibid. **64**: 101, 1947. Jungeblut, C. W., and Bourdillon, J.: Electromicrography in Murine Poliomyelitis Virus Preparations. J. A. M. A. **123**: 399 (Oct. 16) 1943.

8. Taylor, A. R.; Sharp, D. G.; Beard, D.; Beard, J. W.; McLean, I. W., Jr.; Dingle, J. H., and Feller, A. E.: J. Immunol. **47**: 261, 1943; **48**: 129 and 361, 1944; South. M. J. **37**: 313, 1944. Henle, W., and Henle, G.: Science **98**: 87, 1943. Chambers, L. A., and Henle, W.: J. Exper. Med. **77**: 251, 1943. Chambers, L. A.; Henle, W.; Lauffer, M. A., and Anderson, T. F.: ibid. **77**: 265, 1943. Stanley, W. M.: ibid. **79**: 267, 1944; **81**: 193, 1945. Williams, R. C., and Wyckoff, R. W. G.: Proc. Soc. Exper. Biol. & Med. **58**: 265, 1945. Mosley, V. M., and Wyckoff, R. W. G.: Nature, London **157**: 263, 1946.

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10. Kausche, G.A., Pfankuch, E., and Ruska, H.: Naturwissenschaften 27: 292, 1939. Melchers, G.: Schramm, G.; Trurnit, H., and Friedrich-Freksa, H.: Biol. Zentralbl. 60: 524, 1940. Stanley, W.M., and Anderson, T.F.: J. Biol. Chem. 139: 325, 1941. Williams, R.C., and Wyckoff, R.W.G.; Science 101: 594, 1945. Wyckoff, R.W.G.: Biochem. et biophys. acta 2: 139, 1947. Sigurgeirsson, T., and Stanley, W.M.: Phytopathology 37: 26, 1947. Crook, E.M., and Sheffield, F.M.L.: Brit. J. Exper. Path. 27: 328, 1946.

11. Bernal, J. D., and Fankuchen, I.: J. Gen. Physiol. **25**: 111, 1941. Wyckoff, R. W. G.: Biochem. et biophys. acta **1**: 139, 1947

12. Price, W. C., and Wyckoff, R. W. G.: Nature, London **157**: 764, 1946. Markham, R.; Smith, K. M., and Wyckoff, R. W. G.: ibid. **159**: 574, 1947.

13. Anderson, T. F., and Stanley, W. M.: J. Biol. Chem. **139**: 339, 1941. Black, L. M.; Price, W. C., and Wyckoff, R. W. G.: Proc. Soc. Exper. Biol. & Med. **61**: 9, 1946.

of virus (of the order of a millionth of a millionth of a gram) suggests that extraordinarily sensitive diagnostic methods may be developed around the use of the electron microscope. Before this can be done, however, it is necessary to have an understanding of the reaction products formed by different antigens at a full range of antigen-antibody ratios. Studies that will result in this knowledge are also providing the basis for a thorough

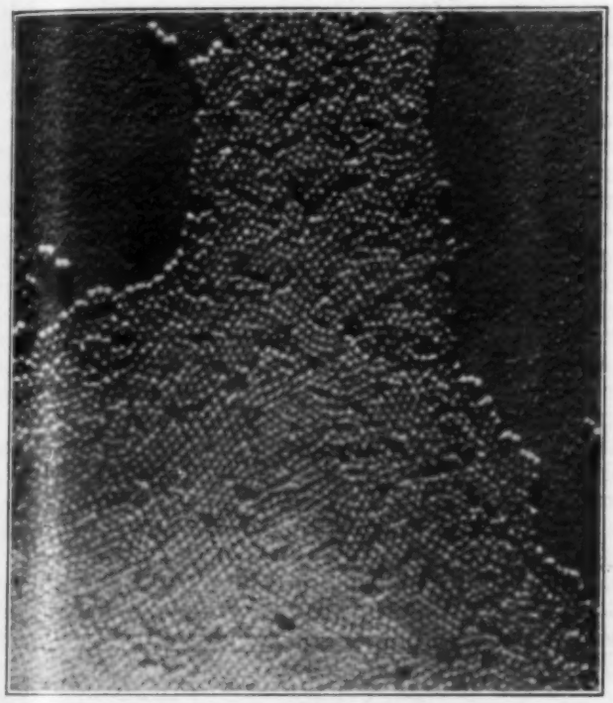

Fig. 3.—Masses of elementary particles on the edge of a desiccated droplet of a purified suspension of the bushy stunt virus. The beginnings of orderliness in particle arrangement, which results in crystal formation, are apparent. Gold shadowing; magnification, 38,000.

evaluation of current theories of the nature of the immune reaction and of the way serum neutralizes and affords protection against viruses and other proteins foreign to an animal.

The ability to recognize virus particles by their characteristic sizes and shapes permits an approach to the extremely important and interesting problem of how they are produced or how they multiply. To do this it is necessary to work with viruses that are not in pure form but are within the cells which they infect. Ultimately this can be done by observing thin sections of cells in various stages of the virus infection. Sections suitable for electron microscopy must, however, be thinner than those that can be cut routinely with conventional microtomes. Special machines[14] having the high speed knives required to cut ultrathin sections are being developed, but much research in the technics of fixing and staining is needed to give them their full usefulness. A tissue can often be examined under the electron microscope without sectioning when it can be induced to grow in tissue culture as a single layer of cells.[15] This should be a fruitful way of studying the inclusion bodies produced by many viruses. The question of virus multiplication can also be approached by choosing host cells that grow singly rather than in a tissue and are small enough not to be opaque in the electron microscope. Bacteria and the bacteriophages that feed on them are probably the simplest systems of this sort. It is not hard to prepare replicas of such systems as they develop on the surface of an ordinary agar plate.[16] My associates and I have been studying the development of a number of bacteriophages in this way. The phenomena are of great complexity, depending, as they do, not merely on the organisms involved but also on their conditions of growth. Gradually, however, we are seeing the steps involved in the process by which a bacterium is converted into a mass of bacteriophage particles and are thereby gaining insight into the mechanism that brings it about.

Not all phages are sperm shaped as are those in figure 1, and they are not all found within the bodies of infected organisms. Often bacterial protoplasm will be almost completely transformed[17] into bacteriophage

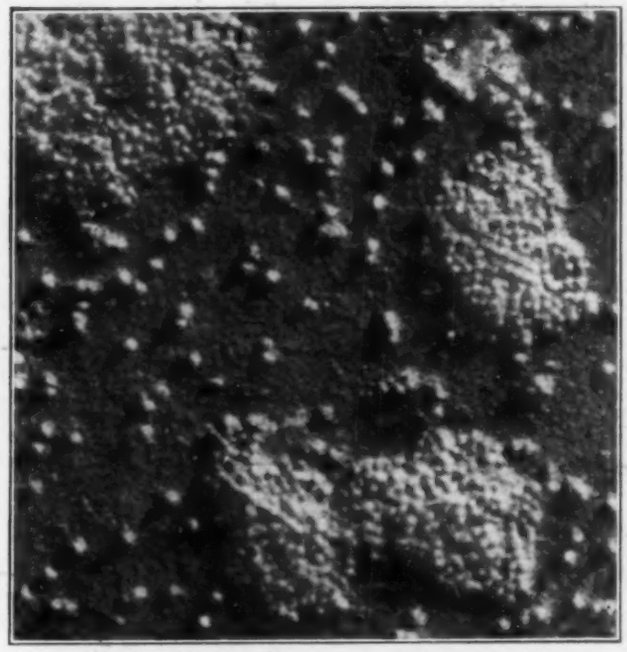

Fig. 4. Several microfloes of bushy stunt virus agglutinated specifically by antiviral rabbit serum. The disordered array of the virus particles in a floc is to be compared with their partially ordered arrangement in such a deposit of pure particles as that shown in figure 3. A gold shadowed replica; magnification, 43,000.

particles according to a pattern of practically crystalline regularity. We are gradually perceiving the implications of such observations for the nature of bacteriophage. With certain systems, lysis leaves behind such diverse particles that it is hard to be certain which of them carries the activity. This is the case for instance with Proteus bacilli, whose plaque areas are rich in multiply flagellated objects. Are these objects carriers of bacteriophage activity and are they perhaps motile "living" objects, too small to be visible in anything but the electron microscope? Information about these and many other novel questions raised by venturing into this hitherto impenetrable world of small objects is important not only to an understanding of viruses and the diseases they produce but to the most basic questions dealing with the nature of the living process itself.

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COMMON VIRUS INFECTIONS OF THE RESPIRATORY TRACT

DIAGNOSIS AND ETIOLOGY

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Knowledge of certain virus infections of the respiratory tract has increased greatly within the short span of the last fifteen years. During this period two distinct types of influenza virus have been isolated and characterized,[1] the large group of immunologically related viruses termed the "psittacosis-lymphogranuloma" group has been more sharply delineated,[2] and important advances have been made in the understanding of contagious diseases, such as measles[3] and mumps,[4] which are due to viruses and are spread by secretions of the respiratory tract. These well known specific infections, however, together comprise the lesser part of the problem of virus infections of the respiratory tract.

The greater part of the problem, in terms of frequency of occurrence of cases,[5] encompasses the group of common infections which vary in their clinical characteristics from the "common cold" to the "atypical pneumonia" and are referred to by a variety of additional names, including "nasopharyngitis," "laryngitis," "grip," "common respiratory disease," "catarrhal fever," "tracheitis" and "bronchitis." A great deal of time and effort have been devoted to investigations of this group of infections, but relatively little is yet known about their interrelationships and causation. While some of the infections have been found to be due to filterable agents, presumably viruses,[6] no one of the agents has been isolated and cultivated in the laboratory in a manner which permits adequate characterization.

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From the Departments of Preventive Medicine and Medicine, Western Reserve University School of Medicine, Cleveland, and the Commission on Acute Respiratory Diseases, Army Epidemiological Board, Office of the Surgeon General, United States Army, Washington, D. C.

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3. Rake, G.: Experimental Investigation of Measles, J. Pediat. **23**: 376 (Oct.) 1943.

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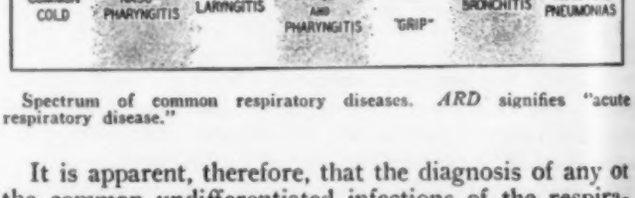
6. (*a*) Kruse, W.: Die Erreger von Husten und Schnupten, Munchen. med. Wchnschr. **61**: 1547, 1914. (*b*) Foster, G. B., Jr.: The Etiology of Common Colds, the Probable Role of a Filterable Virus as the Causative factor with Experiments on the Cultivation of a Minute Micro-Organism from the Nasal Secretion Filtrate, J. Infect. Dis. **21**: 451 (Nov.) 1917. (*c*) Dochez, A. R.; Shibley, G. S., and Mills, K. C.: Studies on the Common Cold: IV. Experimental Transmission of the Common Cold to Anthropoid Apes and Human Beings by Means of a Filterable Agent, J. Exper. Med. **52**: 701-716 (Nov.) 1930. (*d*) Long, P. H.; Doull, J. A.; Bourn, J. M., and McComb, E.: The Etiology of Acute Upper Respiratory Infection (Common Cold), ibid. **53**: 447-470 (April) 1931. (*e*) Experimental Transmission of Minor Respiratory Illness to Human Volunteers by Filter-Passing Agents: I. Demonstration of Two Types of Illness Characterized by Long and Short Incubation Periods and Different Clinical Features, Commission on Acute Respiratory Diseases, J. Clin. Investigation **26**: 957-973 (Sept.) 1947. (*f*) II. Immunity on Reinoculation with Agents from the Two Types of Minor Respiratory Illness and from Primary Atypical Pneumonia, Commission on Acute Respiratory Disease, J. Clin. Investigation **26**: 974-982 (Sept.) 1947. (*g*) The Present Status of the Etiology of Primary Atypical Pneumonia, Commission on Acute Respiratory Disease, Bull. New York Acad. Med. **21**: 235-262 (May) 1945.

Much has been written about diseases of the respiratory tract due to the viruses of influenza, psittacosis and other well characterized agents. It is the purpose of this paper to consider the present status of the diagnosis and etiology of those common infections whose differentiation and classification are as yet ill defined.

GENERAL CONSIDERATIONS

From the standpoint of clinical diagnosis the various common forms of mild infection of the respiratory tract present a major problem, both with respect to segregating them as a group from those due to known specific viruses and bacteria, and with regard to separating, one from another, the possible entities within the group. In part at least, this difficulty arises from the relatively limited capacity of tissues of the respiratory tract to react to the presence of any noxious agent. While single or multiple symptoms and signs may be almost pathognomonic for infection with a few known agents, the clinical picture in the majority of patients is dependent on nonspecific features, such as congestion, edema, altered secretory activity of the mucosal cells, leukocytic infiltration and, in some instances, necrosis and formation of a membrane. In addition, the constitutional reactions of fever, chilliness or rigor, aching, and malaise may have varying degrees of prominence. Thus the clinical picture depends on which of these features are predominant. More than one agent may produce the same clinical type of illness, and, in addition, a single agent, such as influenza virus A, may induce diverse clinical pictures simulating almost any of the common diseases of the respiratory tract.[7]



Spectrum of common respiratory diseases. *ARD* signifies "acute respiratory disease."

It is apparent, therefore, that the diagnosis of any of the common undifferentiated infections of the respiratory tract can now be made with certainty only by the exclusion of diseases of known cause, such as tuberculosis, diphtheria, beta hemolytic streptococcus infections, influenza and psittacosis. When such exclusion has been carried out, there remain a large number of cases which can be grouped in a "clinical spectrum" according to the predominant features of the cases (figure). Obviously, this arrangement is an artificial one based on fever and other factors contributing to severity of illness, on the anatomic location of the principal symptoms and signs and, in one instance, on a single sign—exudate—present on the tonsils or the pharyngeal wall. It is impossible to draw sharp lines between these groups, which clinically shade into one another and vary within themselves. Such a classification, however, does provide a means of selecting cases by clinical criteria for the study of causation and the separation of etiologic entities. While not all of the groups named have been investigated sufficiently to warrant more than the foregoing mention, evidence is now available which suggests that four of these categories may represent separate etiologic entities, namely, the "common cold," nonbacterial exudative pharyngitis

7. (*a*) Hare, R.; Hamilton, J., and Feasby, W. R.: Influenza and Similar Respiratory Infections in a Military Camp Over a Period of Three Years, Canad. J. Pub. Health **34**: 453-464 (Oct.) 1943. (*b*) Stuart-Harris, C. H.: Influenza Epidemics and the Influenza Viruses, Brit. M. J. **1**: 209 (Feb. 17) 1945.

and tonsillitis, "acute respiratory disease" (*ARD*) and primary atypical pneumonia.

"COMMON COLD"

The "common cold" is usually defined as a mild, self-limited, afebrile respiratory illness, characterized by catarrhal inflammation of the mucous membranes of the nose, the sinuses and contiguous structures of the upper respiratory passages. The prominent features diagnostically are coryza, lacrimation, a dry and scratchy throat, an irritative cough, swollen and congested nasal mucous membranes and a normal leukocyte count. But considerable clinical variations are seen in "colds" as they occur in different persons and in the same person at different times. Some appear to be localized in the nose and the sinuses, or the throat; others, regardless of the area of initial involvement, spread to affect almost the entire respiratory tract. Some are mild, without systemic reactions; others are more severe, with associated fever, chilliness, malaise and other constitutional symptoms. Clinically, then, the diagnosis of "common cold" encompasses illnesses which may represent variations of a single disease entity or which may be due to multiple agents.

The investigations of Kruse, Foster, Dochez, Long and their respective co-workers[6a-d] demonstrated that coryzal types of illness with a short period of incubation could be transmitted to well human beings and chimpanzees by inoculation of bacteria-free washings of the respiratory tracts of patients with "colds." Recent investigations of the Commission on Acute Respiratory Diseases[6e, f] have confirmed and extended these studies. Mild, afebrile coryzal infections of the upper respiratory tract were induced in volunteers by inoculation of bacteria-free filtrates of throat washings from each of two donor subjects. One of these donors experienced a moderately severe illness—termed a "severe common cold"—characterized by low grade fever, sneezing, profuse coryza, productive cough and the constitutional symptoms of feverishness, headache, malaise and anorexia. The nasal mucous membranes were injected and edematous, and there was mild hypertrophy of the pharyngeal lymphoid follicles. No abnormal signs were present in the chest. The lungs and the sinuses appeared to be normal on roentgenographic examination. Leukocyte counts were 11,800 and 9,700 on the second and the fifth day, respectively. Cultures of pharyngeal material and sputum revealed no significant pathogenic bacteria. The duration of illness was sixteen days. The other donor suffered a mild illness, without fever, but with dryness and irritation of the throat, nasal obstruction and discharge, sneezing, hoarseness and a dry cough. Physical examination revealed only congestion and edema of the nasal mucous membranes. Roentgenographic examination of the lungs and the sinuses, and other laboratory studies revealed no abnormalities. The illness lasted approximately five days and was termed a "common cold."

Mild, afebrile illnesses, characterized principally by sneezing, coryza and nasal obstruction, were produced in approximately two thirds of each group of volunteers inoculated with filtered washings from these two donors. Symptoms developed within twenty-four to forty-eight hours after administration of the inoculums. Physical examination revealed injection and swelling of the nasal mucous membranes, associated with nasal discharge. Despite the differing clinical characteristics of the illnesses in the two donors, there were no recognizable differences in the infections induced by the respective inoculums. Repeated cultures of material taken from the throats of the recipients before and after inoculations showed no unusual changes in the character of the bacterial flora. The duration of the illnesses was approximately seven to ten days in each group.

As a control, each of a group of 9 men was inoculated with an autogenous washing, similarly collected and filtered. In none of these men did any symptoms or signs of infection develop during the following thirty days. It was therefore concluded that the procedure of inoculation was not in itself responsible for the results obtained.

In an attempt to define further the nature of the infections induced by the "common cold" inoculums, certain of the volunteers were reinoculated with the same or with homologous filtrate after an interval of approximately three weeks. Coryzal illnesses again developed within twenty-four to forty-eight hours, indicating the absence of active immunity under these conditions of exposure. A lack of heterologous immunity also was shown by the occurrence of illnesses following subsequent inoculations made in these men at successive intervals with two heterologous washings obtained in cases of "acute respiratory disease" and primary atypical pneumonia.

It would therefore appear that coryzal illnesses resembling the "common cold" and having an incubation period of one to two days can be transmitted to human subjects by the administration of filtered secretions of the respiratory tracts of patients whose clinical illnesses differ at least in severity, if not in other respects. Presumably the causative agents are viruses. Further investigations are necessary to determine whether or not single or multiple agents are involved, to evaluate more fully the apparent lack of active immunity and to develop specific diagnostic tests.

NONBACTERIAL EXUDATIVE TONSILLITIS AND PHARYNGITIS

The occurrence of cases of nonbacterial exudative tonsillitis and pharyngitis has been observed by a number of investigators,[8] particularly in geographic areas having a relatively low incidence of beta hemolytic streptococcus infections. In certain studies[8e-f] the frequency of occurrence of respiratory illnesses associated with pharyngeal or tonsillar exudate not attributable to bacteria has been three times as great as that of illnesses due to streptococci or other bacteria.

Nonbacterial exudative tonsillitis and pharyngitis is generally a mild disease of short duration. The onset is ordinarily gradual, and the early complaints of the majority of patients are those of feverishness, headache and anorexia. Symptoms of sore throat, hoarseness and cough, often productive, are noted by

8. (*a*) Stuart-Harris, C. H.; Andrewes, S. H.; Smith, W.; Chalmers, D. K. M.; Cowen, E. G. H., and Hughes, D. L.: A Study of Epidemic Influenza, with Special Reference to the 1936-1937 Epidemic, Medical Research Council, London, His Majesty's Stationery Office, 1938. (*b*) Francis, T., Jr.: Epidemic Influenza: Studies in Clinical Epidemiology, Ann. Int. Med. **13**: 915-922 (Dec.) 1939. (*c*) Endemic Exudative Pharyngitis and Tonsillitis: Etiology and Clinical Characteristics, Commission on Acute Respiratory Diseases, J. A. M. A. **125**: 1163-1169 (Aug. 26) 1944. (*d*) Role of β-Hemolytic Streptococci in Common Respiratory Disease, Commission on Acute Respiratory Diseases, Am. J. Pub. Health **35**: 675-682 (July) 1945. (*e*) Keith, J. D., and Carpenter, J.: The Diagnosis of Haemolytic Streptococcal Infection in Acute Nasopharyngitis, Canad. J. Pub. Health **37**: 127-139 (April) 1946. (*f*) Exudative Tonsillitis and Pharyngitis of Unknown Cause, Commission on Acute Respiratory Diseases, J. A. M. A. **133**: 588-593 (March 1) 1947.

75 per cent or more of the patients and tend to reach great prevalence by the third or fourth day of illness. Nasal symptoms are not prominent. On physical examination the mucous membranes of palate, pharyngeal wall and tonsils show varying degrees of injection, which usually is not severe. The exudate is ordinarily small in amount and appears as gray or yellow individual spots which are pinhead in size. Larger patches of exudate may develop, but rarely do they become confluent. Often the exudate forms over swollen lymphoid follicles on the pharyngeal wall. Cervical lymphadenopathy may be present in approximately one fourth of the cases. Involvement of the lungs occasionally occurs.[9] In approximately two thirds of the cases the total leukocyte counts are below 10,000 and the differential formulas are normal. Bacteriologic and serologic examinations give no evidence of beta hemolytic streptococcus infection. The average peak of temperature is between 101 and 102 F, and the fever ordinarily declines by lysis. The duration of illness is approximately five days, and convalescence is usually uneventful.

The cause of this syndrome has not been determined, nor have direct attempts been made to transmit the infection in man. It is worth mention, however, that in the experimental transmission of primary atypical pneumonia and minor respiratory illness to human volunteers, pharyngeal or tonsillar exudate of minimal degree was present in 2 cases of pneumonia and in 2 cases of minor illness.[10] Whether a single agent or more than one agent was active in these cases cannot be determined, however, because the particular inoculum given these persons was not filtered and consisted of specimens pooled from several donors. At the present time the disease can be diagnosed only after the exclusion, by cultural and serologic methods, of the common bacterial infections. While it is recognized that exudate is not necessarily pathognomic of a specific infection, a brief description of the syndrome of nonbacterial exudative tonsillitis and pharyngitis has been presented here because this condition may represent an etiologic entity among the common virus infections of the respiratory tract.

"UNDIFFERENTIATED ACUTE RESPIRATORY DISEASE"

It has long been common knowledge in military circles that recruits are highly susceptible to disease of the respiratory tract during their first few weeks of training. Experiences of the past war have confirmed this observation [11] and, in addition, have shown that the bulk of those illnesses which require hospitalization appear to represent an epidemiologic and clinical entity which for lack of a better term has been called "undifferentiated acute respiratory disease" by the Commission on Acute Respiratory Diseases.[11b] Epidemiologically this type of illness has shown a constant pattern of behavior during three years of observations. Epidemics have occurred in recruits with regularity during the winter months.[11b] Clinically the diagnosis has been made by the exclusion of bacterial infections, influenza A and B, exudative lesions of pharynx or tonsils, and pneumonia. While this syndrome has been recognized in military populations, there is no reason to believe that it does not also occur in civilians.[8a,b]

The clinical picture of "undifferentiated acute respiratory disease," as seen in hospitalized recruits is that of a mild respiratory illness of gradual onset. The most frequent complaints are those of feverishness, chilliness and headache. Symptoms of malaise, anorexia and nasal involvement occur in approximately half of the patients. Sore throat is common but is mild in degree in comparison with that encountered in patients having exudate in the throat. Minimal hoarseness and cough are common, although fewer than half of the patients have a productive cough or pain in the chest. On physical examination the patients rarely appear to be severely or even moderately ill. Physical signs are remarkably few and are usually noted in less than half of the patients. Nasal obstruction, mild injection of pharynx and palate, and lymphoid hyperplasia on the pharyngeal wall are most frequently found. Edema of the mucous membranes, cervical adenopathy and thoracic rales are present in approximately 10 per cent of the patients. The febrile course is short, from two to four days, and the average maximum temperature is about 101 F. Constitutional symptoms subside with defervescence, but symptoms referable to the respiratory tract, when present, tend to persist for one or two weeks. Leukocyte counts are usually within normal limits, and cultures of the throat reveal only normal bacterial flora.

It therefore appears that the syndrome of "undifferentiated acute respiratory disease" may be a clinical entity of nonbacterial origin, which differs from the "common cold" or acute coryza. Attempts to isolate the causative agent in animals have been unsuccessful. Mild respiratory illnesses have been transmitted to human volunteers, however, by means of filtered throat washings from a representative donor.[6e,f] Fourteen of 19 men inoculated became ill, and in 10 of the 14 patients symptoms first appeared on the fifth or sixth day after inoculation. While the clinical pattern was somewhat variable, the initial complaints were usually those of dryness or soreness of the throat which developed gradually during the course of twenty-four or forty-eight hours. Constitutional symptoms were minimal or absent; nasal symptoms were of minimal intensity and not associated with coryza. Mild inflammation of palate and pharynx and lymphoid hyperplasia were the only noteworthy signs on physical examination. The course of illness in general was mild and afebrile, and the duration of symptoms varied from four to twelve days. Laboratory studies yielded normal results.

Reinoculation of 6 of these men with filtered washings from the same donor produced no illness. It thus appeared that "undifferentiated acute respiratory disease," in contrast with the "common cold," was followed by homologous active immunity. Successive inoculations of these men, at later periods, with filtrates of throat washings from the patient with "severe common cold" and from a patient with primary atypical pneumonia, however, failed to demonstrate heterologous immunity to the agents producing the latter two types of respiratory disease.

This study in human volunteers indicates that a mild disease of the respiratory tract characterized by

9. Association of Acute Pulmonary Lesions with Infections of the Throat, Commission on Acute Respiratory Diseases, Ann. Int. Med. **25**: 475-487 (Sept.) 1946.

10. The Transmission of Primary Atypical Pneumonia to Human Volunteers, Commission on Acute Respiratory Diseases, Bull. Johns Hopkins Hosp. **79**: 97-167 (Aug.) 1946.

11. (*a*) Krueger, A. P., and others: The Diagnosis of Influenza and Acute Catarrhal Fever, U. S. Nav. M. Bull. **42**: 27-33 (Jan.) 1944. (*b*) Acute Respiratory Disease Among New Recruits, Commission on Acute Respiratory Diseases, Am. J. Pub. Health **36**: 439-450 (May) 1946. (*c*) Clinical Pattern of Undifferentiated and Other Acute Respiratory Diseases in Army Recruits, Commission on Acute Respiratory Diseases, Medicine **26**: 441-464 (Dec.) 1947. (*d*) Hare and others.[7a]

an incubation period of five to six days and predominance of pharyngeal symptoms and signs can be transmitted in man. The disease not only has a longer period of incubation than the "common cold" but also appears to be immunologically distinct. The causative agent is filterable and is presumed to be a virus. The evidence now available suggests that this experimentally induced illness is the same as the "undifferentiated acute respiratory disease" of recruits, but final acceptance of this relationship must await isolation of the virus and the development of specific serologic tests for confirmation of the diagnosis.

PRIMARY ATYPICAL PNEUMONIA

Within the past ten years primary atypical pneumonia has become the commonest form of pneumonia, in terms of frequency of occurrence, and has been the subject of numerous reports and reviews.[12] Only limited consideration, therefore, will be given here to its diagnosis and etiology.

Primary atypical pneumonia is an acute disease of the respiratory tract or a syndrome characterized chiefly by gradual onset, benign course and diffuse or patchy pulmonary infiltration demonstrable by roentgenogram. In some patients the constitutional symptoms of headache, feverishness, chilliness, malaise and fatigue are prominent in the early stages of illness and gradually increase in severity. In others, the illness begins as a localized infection of the respiratory tract, as indicated by dryness and soreness of the throat and by cough, and constitutional symptoms develop either simultaneously or after several days of illness. Coryza may be noted in about one third of the cases. As the disease progresses, the cough ordinarily becomes productive of greenish yellow mucopurulent sputum. Rarely is the sputum intimately mixed with blood. Substernal pain of a dull character commonly accompanies the cough. Physical examination early in the illness usually reveals little beyond mild infection of the pharynx. Later, however, medium fine, sticky rales and coarse rales are characteristically heard over the involved area of the lungs. The classic signs of consolidation—dulness, increased tactile fremitus and altered breath and voice sounds—are rarely observed.

Roentgenographic examination frequently provides the first evidence of pulmonary involvement. The infiltration is usually light and patchy in character and peribronchial in distribution, compatible with the pathologic changes of interstitial pneumonia, lobular atelectasis and necrotizing bronchiolitis. The process may begin at the hilus or in the parenchyma of the lung. The lower lobes are most frequently involved, but any portion of the lung may be affected. In general, diffuse involvement, particularly of the upper lobes, is found in the more severely ill patients.

The usual clinical laboratory examinations yield results which are within normal limits. The total leukocyte count is ordinarily less than 10,000, and the differential formula is normal. Urinary changes, if present, are those compatible with any febrile illness. Cultures of the sputum and of the throat show the normal occurrence and distribution of the bacterial flora of the respiratory tract.

The course of the average illness is benign and of approximately five to seven days' duration. Complications are infrequent, and the prognosis is excellent, despite the lack of specific therapy.

Thus, the characteristics of primary atypical pneumonia are such that a definite diagnosis may at times be extremely difficult if not impossible to establish on the clinical features alone. It may be necessary to exclude, by the appropriate diagnostic procedures, a number of diseases of known cause which may present essentially the same syndrome, such as tuberculosis, tularemia, bacterial pneumonia, coccidioidomycosis, Q fever, psittacosis and influenza.

While the diagnosis of primary atypical pneumonia is still one of exclusion, two laboratory tests are of some help. Both of these tests are agglutination reactions in which acute and convalescent phase specimens of the patient's serum should be examined in order to demonstrate a rise in antibody titer. The first or "cold hemagglutination" test[13] utilizes group O human red blood cells as antigen, and the reaction occurs only at a cold (usually icebox) temperature. On warming to 37 C. the hemagglutinin disappears. The second test is the agglutination of Streptococcus MG[14] and is carried out in essentially the same fashion as other bacterial agglutination tests. The proportion of patients whose serums show significant increases in titer for one or the other of these agglutinating antibodies or for both has varied in the several reported series of cases, but, in general, approximately 50 per cent of the patients show development of the antibodies.[12e] The two reactions appear to be directly correlated with severity of illness and extent of pulmonary involvement. It should be emphasized that each test provides only a restrospective confirmation of the diagnosis of primary atypical pneumonia, since the antibodies do not develop until the second or third week of illness. Moreover, failure to demonstrate the antibodies does not exclude the diagnosis.

The causation of primary atypical pneumonia was extensively investigated in a number of laboratories during the war. Attempts to establish in animals an infection which could be related immunologically to the human disease have for the most part been unsuccessful.[15] Eaton and his co-workers,[16] however, have reported that pulmonary lesions were produced in cotton rats and hamsters by intranasal administration of bacteria-free suspensions prepared from chick embryos previously inoculated with specimens from patients with primary atypical pneumonia. That the agent is neutralized by convalescent serums has been reported in approximately 60 per cent of cases of primary atypical

12. (*a*) Dingle, J. H., and Finland, M.: Virus Pneumonias: II. Primary Atypical Pneumonias of Unknown Etiology, New England J. Med. **227:** 378-385 (Sept. 5) 1942. (*b*) Reimann, H. A.: Viral Pneumonias, Bull. New York Acad. Med. **19:** 177-182 (March) 1943. (*c*) MacLeod, C. M.: Primary Atypical Pneumonia, M. Clin. North America **27:** 670-686 (May) 1943. (*d*) Primary Atypical Pneumonia, Commission on Acute Respiratory Diseases, Am. J. Pub. Health **34:** 347-357 (April) 1944. (*e*) Horsfall, F. L., Jr.: Primary Atypical Pneumonia, New York State J. Med. **46:** 1810-1814 (Aug. 15) 1946.

13. Peterson, O. L.; Ham, T. H., and Finland, M.: Cold Agglutinins (Autohemagglutinins) in Primary Atypical Pneumonias, Science **97:** 167 (Feb. 12) 1943. Turner, J. C.: Development of Cold Agglutinins in Atypical Pneumonia, Nature, London **151:** 419-420 (April 10) 1943.

14. Thomas, L.; Mirick, G. S.; Curnen, E. C.; Ziegler, J. E., Jr., and Horsfall, F. L., Jr.: Serological Reactions with an Indifferent Streptococcus in Primary Atypical Pneumonia, Science **98:** 566-568 (Dec. 24) 1943. Thomas, L.; Mirick, G. S.; Curnen, E. C.; Ziegler, J. E., Jr., and Horsfall, F. L., Jr.: Studies on Primary Atypical Pneumonia: II. Observations Concerning the Relationship of a Non-Hemolytic Streptococcus to the Disease, J. Clin. Investigation **24:** 227-240 (March) 1945.

15. Commission on Acute Respiratory Diseases,[4g] Horsfall.[12e]

16. (*a*) Eaton, M. D.; Meicklejohn, G., and van Herick, W.: Studies on the Etiology of Primary Atypical Pneumonia: A Filterable Agent Transmissible to Cotton Rats, Hamsters, and Chick Embryos, J. Exper. Med. **79:** 649-668 (June) 1944. (*b*) Eaton, M. D., and van Herick, W.: Serological and Epidemiological Studies on Primary Atypical Pneumonia and Related Acute Upper Respiratory Disease, Am. J. Hyg. **45:** 82-95 (Jan.) 1947.

pneumonia and 20 per cent of cases of the undifferentiated infection of the upper respiratory tract.[16b]

Studies of the Commission on Acute Respiratory Diseases[10] have demonstrated that primary atypical pneumonia can be transmitted to and passed in human volunteers by means of bacteria-free filtrates of sputum and throat washings. In approximately one fourth of the volunteers respiratory illnesses developed, with pulmonary infiltration being demonstrated roentgenographically. Clinically the experimentally induced infections resembled the naturally acquired disease. The average period of incubation was ten to twelve days. There was no evidence that bacteria played any part in initiating the infections or during the course of the disease.

The clinical and the experimental evidence thus indicate that primary atypical pneumonia is a virus infection of the respiratory tract. Further investigation is necessary, however, to determine whether or not one agent or more than one is concerned in the production of the naturally acquired disease.

CONCLUSIONS

In conclusion, the outstanding problem in the field of diseases of the respiratory tract relates to the common infections of the respiratory tract which are so frequent in occurrence and which appear to vary in type from the "common cold" at one extreme to "atypical pneumonia" at the other. These infections are thought to be caused by viruses as yet uncharacterized, but they may be segregated into a group at the present time only by the exclusion of cases due to the known bacteria and viruses. Clinical classification is unsatisfactory at best, since it is based mainly on severity, extent of involvement of the respiratory tract and prominence of localizing symptoms and signs. An attempt at differentiation, however, has been useful as a means of selecting cases for etiologic investigation. It now appears probable that three entities, termed the "common cold," "undifferentiated acute respiratory disease" and "primary atypical pneumonia," can be separated from the larger group. Each of them can be transmitted to well human beings by the inoculation of bacteria-free filtrates of secretions of the respiratory tract. The possible existence of a fourth entity, "nonbacterial exudative tonsillitis and pharyngitis," is indicated by clinical studies.

The Campaign Against Rheumatism.—In every country surveyed the same findings have been made: (1) rheumatic diseases outranked all others as a cause of chronic morbidity; (2) rheumatic diseases annually involve each country in great expense; (3) adequate facilities for the care of most rheumatic patients are nonexistent. In the United States as elsewhere the total army of rheumatic victims is relatively neglected. Compare their prospects with that of others, for example, the tuberculous: for our 680,000 tuberculous patients there are available about 100,000 free beds and $100,000,000 for care and research. But for our 6,850,000 rheumatic patients there are available only about 200 free beds and $200,000 for care and research. In other words, although there are 10 times as many rheumatic as tuberculous patients the latter have available 500 times more beds and money. Thus the tuberculous patient, happily thereby a "vanishing race," receives 5,000 times as much attention as the nonvanishing rheumatic.—Hench, P.S.: *Annals of Internal Medicine*, February, 1948.

SEARCH FOR EXTRAHUMAN SOURCES OF POLIOMYELITIS VIRUS

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The best evidence of the transmission of the virus of poliomyelitis at the present time supports a person to person transfer. In spite of the logic of this thesis, based essentially on the well known fact that virus is present in the human oropharynx and intestinal tract for varying periods, one must not forget that the evidence was arrived at through processes of elimination rather than by scientifically proved experiments. Consequently, it is difficult, if not impossible, in determining the transmission of this disease, to rule out extrahuman factors completely, especially since epidemiologic observations have emphasized for years that outbreaks of poliomyelitis are correlated with seasonal influences, such as rainfall, temperature and prevalence of insects and animals.

In reviewing the literature on this subject one is impressed by the vast number of incriminations of various extrahuman factors, based at best on epidemiologic impressions gained through observations of limited accuracy, and also by the paucity of reports, either positive or negative, in which it is indicated that confirmation has been sought through actual investigation. Thus, the value to other investigators of the reporting of negative results is emphasized by the fact that so few reports on this subject exist.

Milk has been condemned in several epidemics, but entirely without laboratory support. Neustaedter and Thro[1] reported that poliomyelitis developed in monkeys infected with dust from a sickroom. Kling[2] and Toomey and his co-workers[3] seem to be the only ones reporting that the virus of poliomyelitis has been isolated from water. Sewage is not truly extrahuman, since it represents human excreta which may contain virus. Virus has actually been found in sewage by Paul, Trask and associates,[4] by Toomey[5] and by Kling and associates.[6] These isolations were almost invariably made from samples taken near the source of outlet and not far from hospitals containing patients with poliomyelitis. Jungeblut

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2. Kling, C.: In Search of Poliomyelitis Virus in Drinking Water, Internat. Bull. Econ. M. Research & Pub. Hyg. **A40**: 161, 1939

3. (*a*) Toomey, J. A.; Takacs, W. S., and Tischer, L. A.: Attempts to Recover Poliomyelitis Virus from Fruit, Well Water, Chicken Cords, and Dog Stools, J. Pediat. **23**: 168, 1943. (*b*) Toomey, J. A.; Takacs, W. S., and Weaver, H. M.: Isolation of Poliomyelitis Virus from Creek Water by Direct Transmission to the Cotton Rat, Am. J. Dis. Child. **70**: 293 (Nov.-Dec.) 1945.

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and associates[7] have reported that rodent-paralyzing agents were isolated from wild mice in several different areas, but considerable doubt exists as to the identity of these strains as agents associated with the human disease. Leake [8] attempted to recover the virus from stools of dogs and chickens, with negative results, as did Toomey and associates,[3a] who also failed to isolate the virus from fish.[9] That the antibodies are present in the serum of animals has been reported by Hammon,[10] Gordon,[11] Brown and Francis [12] and others, but it is significant that the serums were tested against only the mouse-adapted Lansing strain of poliomyelitis virus. The significance of these observations in terms of specific virus effect is not established.

The possibility that some insect plays a role in the transmission remains the most likely of all the extrahuman prospects. Rosenau and Brues [13] and Anderson and Frost [14] reported experimental transmission with the biting fly, Stomoxys calcitrans, but were unable to repeat their results a year later.[15] Sawyer and Herms [16] likewise were unsuccessful with this insect, as was Francis [17] with another biting fly, Lyperosia irritans. Howard and Clark [18] reported negative results of experiments with mosquitoes and lice, and Kling and Levaditi [19] found that flies and bedbugs were negative for virus. Simmons, Kelser and Cornell [20] and Cornell and Davis [21] were unable to transmit infection from monkey to monkey with the mosquitoes Aedes aegypti and Culex pipiens.

Flexner and Clark [22] and Howard and Clark [18] reported that monkey cord virus survived in the housefly, Musca domestica, for several days. Bang and Glaser [23] found that the Lansing strain of virus persisted in the housefly for two days but not in species of Lucilia, Muscina, Calliphora or Sarcophaga. The housefly yielded a strain of spontaneous mouse encephalomyelitis virus twelve days after feeding on the virus. The virus was not isolated from adults when the larvae were infected. Rendtorff and Francis [24] also reported that the Lansing strain was recovered from houseflies as long as two days after a single meal of virus but observed a marked decrease of this virus with time, indicating no multiplication of the agent. The virus was shown to be in the fly and to be excreted in the fecal and vomit spots.

Various workers have recently reported that the virus of poliomyelitis was isolated from captured wild flies —Paul and associates,[25] Toomey and co-workers,[26] Sabin and Ward [27] and Trask and associates.[28] A significant observation was reported by Ward, Melnick and Horstmann,[29] who exposed food to flies in an epidemic area and then fed it to chimpanzees. In these animals infection developed without clinical disease but with persistence of the virus in the gastrointestinal tract.[30]

In this laboratory, in the course of investigating epidemics of poliomyelitis during the past five years, attempts have been made to evaluate the significance of some of the possible extrahuman sources of virus. The efforts to be reported here represent attempts to isolate the virus from various materials, serologic studies to detect antibodies for the virus of poliomyelitis in animals and laboratory experiments with insects.

ATTEMPTS TO ISOLATE THE VIRUS

Mice.—Six pools of mice, representing 33 animals, have been tested for the presence of virus. The mice were captured in or near the homes of patients in three epidemic areas, Michigan, in 1942,[31] and Fort Worth and Texarkana, Texas, in 1943.[32] One animal appeared to be paralyzed. Nervous tissue and several inches of the lower part of the intestine were ground with alundum and filtered through Mandler candles. The bacteriologically sterile filtrates were inoculated intracerebrally in rhesus monkeys, white Swiss mice and cotton rats. No specimen produced signs of the disease.

Rats.—The nervous and intestinal tissues of 112 wild rats, rattus norvegicus, have been tested.[33] The animals were obtained from epidemic areas in rural districts of Michigan, in Texas and in Buffalo and Detroit. Mandler filtrates of 35 pools representing the total number of rats were inoculated intracerebrally in rhesus monkeys, Swiss mice and cotton rats. All specimens failed to transmit infection, with the exception of one pool of brains, cords and intestines from rats captured at the city dump in Fort Worth, Texas, in 1943.[32] A Mandler

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31. (*a*) Pearson, H. E., and Rendtorff, R. C.: Studies of the Distribution of Poliomyelitis Virus: I. In the Environment of Sporadic Cases, Am. J. Hyg. **41**: 164, 1945; (*b*) II. In a Small Town, ibid. **41**: 179, 1945.

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33. Brown and Francis,[32] Pearson and Rendtorff,[31] Pearson and others.[32]

filtrate of the ground tissues from these animals produced paralysis in 1 of 2 cotton rats on the ninth day and in 1 of 6 mice on the thirtieth day. A rhesus monkey inoculated intracerebrally with the same original suspension had marked weakness of both legs and slight weakness of both arms by the ninth day. On autopsy of this animal some neuronophagia and neuronolysis was observed, but an attempt to pass the infection to a second monkey was unsuccessful. The brain and cord of the paralyzed mouse was passed to 4 cotton rats and 10 mice. Paralysis developed again in 1 cotton rat, but further passage was unsuccessful. However, the agent was passed in 9 successive mouse inoculations, inciting typical hind- or foreleg paralysis in the animals. Unfortunately, the percentage of mice in which paralysis developed never exceeded 20 to 25, making it impossible to identify the agent by means of the technic of cross immunization or cross neutralization. The strain has been preserved, and further attempts are being made.

Muskrats.—Three muskrats inhabiting the waters of Three Rivers, Mich., during the epidemic of 1946 were trapped. The rivers in this area were excessively contaminated with fecal material since they received raw sewage from the entire town. The pooled brains and cords and individual suspensions of the intestines of these animals were inoculated intracerebrally in 2 cotton rats and 15 white mice. No signs were observed in the test animals.

Chickens.—Chicken droppings were collected in two epidemic areas of rural Michigan[31] and in Fort Worth, Texas,[32] where chickens represented the major animal species apart from man. Four pools were rendered bacteriologically sterile and were then inoculated intracerebrally and intranasally in rhesus monkeys. All pools failed to produce signs of virus infection.

On four occasions chickens which were limping or were totally unable to walk were observed in yards of homes where poliomyelitis was occurring. Histories revealed that several other chickens had recently died after being lame for a period. The brains and spinal cords were removed aseptically, ground in a mortar and inoculated intracerebrally in white mice. In none of these mice did signs develop.

Cows.—Seven pools of cow feces, representing four epidemic areas, three in Michigan and one in Texas,[34] were processed for intracerebral and intranasal inoculation of rhesus monkeys. One of the cows had a history of recent lameness. All specimens failed to produce signs of virus infection.

Hogs.—Droppings from hogs which were maintained by households in which the disease occurred were collected on two occasions.[31a] Four pools of ether-treated feces were inoculated intracerebrally and intranasally in rhesus monkeys, with negative results.

TABLE 1.—*Attempts to Isolate Virus from Naturally Caught Flies*

Pool	Type of Fly	Flies	Source	Type of Monkey Inoculated	Route *	Result †
1	Miscellaneous	57	Ohio	Rhesus	i.p., i.n.	—
2	Miscellaneous	150	Ohio	Java	i.p., i.n.	—
3	Sarcophagidae	56	Texas	Cebus	i.c.	—
4	Calliphoridae	43	Texas	Cebus	i.c.	—
5	Musca domestica	52	Texas	Cebus	i.c.	—
6	Sarcophagidae	200	Texas	Cebus	i.c., i.n.	—
7	Sarcophagidae	125	Texas	Cebus	i.c., i.n.	—
8	Calliphoridae	57	Texas	Cebus	i.c.	—
9	Musca domestica	127	Texas	Cebus	i.c., i.n.	—
10	Call. and Mus. dom.	34	Texas	Cebus	i.c., i.n.	—
11	Sarc., Call., Mus. dom.	67	Texas	Cebus	i.c., i.n.	—
12	Sarc., Call., Mus. dom.	95	Texas	Cebus	i.c., i.n.	—
13	Sarc., Call., Mus. dom.	140	Texas	Cebus	i.c., i.n.	—
14	Sarc., Call.	210	Texas	Cebus	i.c., i.n.	—
15	Sarc., Call., Mus. dom.	223	Texas	Rhesus	i.c., i.p.	? —
16	Sarc., Call., Mus. dom.	251	Texas	Rhesus	i.c., i.p.	? —
17	Sa., Ca., M. dom., Tabanus, Stomoxys calcitrans	759	Mich.	Rhesus	i.c., i.p.	? —
18	Stomoxys calcitrans	1,000	Ohio	Rhesus	i.c., i.p.	—
19	Sa., Ca., M. dom., Fannia	1,000	Ohio	Rhesus	i.c., i.p.	—
20	Sarc., Call., Mus. dom.	345	Ark.	Rhesus	i.c., i.n.	—
21	Musca domestica	757	Ark.	Rhesus	i.c., i.p.	—
22	Calliphoridae	241	Ark.	Rhesus	i.c., i.p.	—
23	Sarcophagidae	389	Ark.	Rhesus	i.c., i.p.	—
24	Sarc., Call., M. dom., Stom.	626	Ohio	Rhesus	i.c., i.p.	—
25	Musca dom., related flies, miscellaneous	41	Mich.	Rhesus	i.c., i.p., i.n.	—
26	Phaenicia sericata	165	Mich.	Rhesus	i.c., i.p., i.n.	—
27	Phormia regina and terrae-novae	17	Tenn.	Rhesus	i.c.	—
28	Phaenicia sericata	452	Tenn.	Rhesus	i.c.	—
29	Phaenicia sericata	115	Tenn.	Rhesus Philippine	i.c. i.c.	— —
30	Phaenicia sericata	572	Tenn.	Rhesus Philippine	i.c. i.c.	— —
31	Sarcophaga spp.	23	Tenn.	Rhesus Philippine	i.c. i.c.	— +
32	Misc. spp.	41	Tenn.	Rhesus Philippine	i.c. i.c.	— —
33	Phaenicia sericata	64	Tenn.	Rhesus Philippine	i.c. i.c.	— —
34	Musca domestica	21	Tenn.	Rhesus Philippine	i.c. i.c.	— —
35	Sarcophaga spp.	30	Tenn.	Rhesus Philippine	i.c. i.c.	— —
36	Sarcophaga spp.	99	Tenn.	Rhesus Philippine	i.c. i.c.	— —
37	Phaenicia sericata	278	Tenn.	Rhesus Philippine	i.c. i.c.	— —
38	Phormia regina and terrae-novae	61	Tenn.	Rhesus Philippine	i.c. i.c.	— —

* The abbreviations are as follows: i.p., intraperitoneal; i.n., intranasal; i.c., intracerebral.
† A negative sign means that the inoculated animals showed no evidence of virus infection; a plus sign, that definite symptoms of poliomyelitis developed after inoculation.

34. Pearson and Rendtorff.[31] Pearson and others.[32]

Horse.—The stool of a horse which had been in close contact with a patient [31a] was tested for virus by intracerebral and intranasal inoculation of a rhesus monkey. No virus was detected.

Cats.—An interesting set of circumstances surrounded a group of three houses on the outskirts of Buffalo during the epidemic of 1944, where observations were being made by Dr. E. M. Bridge and Dr. E. Neter. In the three houses there occurred 1 definite case of poliomyelitis and 3 cases of minor illness which may have been abortive poliomyelitis. Two children had recently visited the homes; in one definite symptoms developed, and in the other, probably the abortive form of the disease. Of 13 cats residing in these homes, 9 had died within the past few weeks, 3 were well and 1 had flaccid paralysis of the legs. Through the cooperation and assistance of Drs. Bridge and Neter, these 4 remaining animals were killed, and the nervous tissue was removed and sent to us; it was then stored in dry ice until tested by intracerebral and intraperitoneal inoculation in a rhesus monkey. The animal remained perfectly well for the test period of thirty days.

Sewage.—Six specimens of sewage, 5 gallon (19 liter) quantities, were obtained in Fort Worth, Texas, during the epidemic of 1943.[32] A sample of raw sewage, a sample of the final effluent and 4 samples representing various areas of the town were chosen. Each sample was concentrated to a volume of approximately 1 quart (1 liter) by lowering the p_H to 4.2 and precipitating with crystalline egg albumin. The concentrates were preserved by freezing until tested. From 100 to 125 cc. of each was treated with ether to remove the bacteria and then inoculated at least twice in rhesus monkeys intraperitoneally and intranasally in 10 cc. and 2 cc quantities, respectively. The specimen from raw sewage was tested in 3 animals. All were negative for virus.

During the epidemic in Denver, 1946, six daily 1 quart samples of sewage were taken from three sources, the hospital outlet, the stream before it entered the treatment plant and the final effluent.[35] Two hundred cubic centimeters of each daily specimen from each location was used for a pool totaling 1,200 cc., which was then concentrated *in vacuo* to 40 cc. After ether treatment, each of the three pools was inoculated twice intracerebrally in 3 rhesus monkeys. All 3 pools gave negative results.

A pool of soil, totaling 80 Gm., from three truck farms irrigated by the Platte River, which contains the final effluent of the entire city of Denver, was suspended to 10 per cent in distilled water and concentrated *in vacuo*. After treatment with ether, the pool was inoculated intracerebrally in 3 rhesus monkeys, which remained well.

Since sludge from the sewage treatment plant is used extensively as fertilizer in and around Minneapolis, 2 specimens were obtained during the epidemic of 1946. A specimen of three year old sludge, which is usually used on farms, and a specimen of fresh sludge, 40 Gm. of each, were suspended in saline solution and treated with ether. Both were inoculated intracerebrally and intraperitoneally in Philippine monkeys. The animals remained well.

Water.—Nine large samples of water, usually several gallons each, were collected from lakes, ponds, rivers and city water supplies near epidemic areas in Cleveland, Akron, Ohio, Fort Worth, Texas, and several small towns of Michigan.[36] Each specimen was evaporated in sausage casings exposed to electric fans until concentrated to approximately 10 per cent of the original volume and then was inoculated intraperitoneally and intranasally in rhesus monkeys. In 2 monkeys symptoms suggesting infection developed, but the second rhesus passage was uneventful. The other inoculations produced no evidence of infection.

One 15 gallon (56 liter) specimen from the wells of the Perrysburg, Ohio, water department was collected over a twenty-four hour period during the epidemic of 1944. The specimen was concentrated *in vacuo* to a volume of 1 liter, while being maintained at a temperature of 40 F. and a p_H between 6 and 7. It was dialyzed and inoculated intracerebrally in white mice and 3 rhesus monkeys. No virus was recovered.

Milk.—Three specimens of raw milk from farms on which poliomyelitis had occurred [31a] were treated with ether and inoculated intracerebrally and intraperitoneally in rhesus monkeys. All the animals remained free of disease.

Insects.—Forty-three pools of insects, representing approximately 15,300 individual insects, trapped in areas under study,[34] have been tested in monkeys. Two pools of ants and two of cockroaches, with estimated numbers of 6,000 and 140, respectively, were obtained from each of two homes in which cases had occurred. A pool of ticks was made up of larvae, nymphs and adults numbering 150 obtained from a woody area frequented by a patient. Thirty-eight pools, representing seven epidemic areas, were made up of flies trapped in or around the residences of persons suffering with the disease. Many pools were made up of single species of flies. In some instances several kinds were included. In all cases the pools were ground in mortars with alundum, shaken with ether for several days and then, if bacteriologically sterile, inoculated intracerebrally as well as intraperitoneally or intranasally in monkeys.

Java, Capuchin, rhesus or Philippine monkeys were employed, and 10 pools were injected into both rhesus and Philippine monkeys. Table 1 demonstrates the results of these tests. It will be seen that, of all the pools of naturally caught flies, only one specimen, consisting of 23 flies from an unsanitary rural area, all in the genus Sarcophaga, was shown to contain the virus. This specimen produced symptoms of poliomyelitis in a Philippine monkey but was negative in a rhesus monkey. Two other specimens of flies caused questionable symptoms in the first animal inoculated, but the agent could not be passed to a second monkey. The results have been thought to be open to criticism in that rhesus monkeys were used for most tests, and the statement has been made that they are insusceptible to fly virus.

In the past a wide variety of flies has been incriminated in the pools which have yielded virus; the actual species involved have usually not been ascertained. Nevertheless, Musca domestica, the common house fly, has not been prominent in the collections, while the blow fly (Calliphora vomitoria) and several other species have been.

The usual assumption has been that flies acquire their contamination from human excreta, but no direct evidence that they do has been presented. A certain significance might be applicable if the species of flies

35. Ziotnik, A. R.: Unpublished data.

36. Francis, T., Jr.; Krill, C. E.; Toomey, J. A., and Mack, W. N.: Poliomyelitis Following Tonsillectomy in Five Members of a Family, J. A. M. A. **119**: 1392 (Aug. 22) 1942. Pearson and Rendtorff,[31] Pearson and others.[32]

which habitually feed on human stools were known. Accordingly, fresh normal adult human stools were placed as bait in cone-shaped fly traps in numerous areas

TABLE 2.—*Species of Flies That Were Trapped with Human Stools as Bait*

	Number Trapped
Phaenicia sericata and a small number of Lucilia spp....	2,048
Phormia regina and Protophormia terrae-novae.....	629
Sarcophaga spp.	616
Muscina stabulans and Muscina assimilis.....	333
Calliphoro erythrocephala and Calliphora vomitoria.....	107
Cynomyopsis cadaverina	29
Musca domestica	17
Stomoxys calcitrans	7
Callitroga macellaria	6
Fannia canicularis	1
Miscellaneous identified and unidentified specimens.....	856

throughout Michigan during a period when poliomyelitis was not prevalent. The field identifications of the collections made are given in table 2.

The same results were obtained from trappings of flies in rural Tennessee during an epidemic where ample opportunity to feed on feces was provided. It was obvious that the "blow," "flesh" and "green bottle" flies, and not the house fly, were abundantly attracted to human excreta as used in our methods of collection. One should not be misled, however, into believing that the house fly is not attracted to human excrement under some circumstances. These data show that the species encountered were those which had been present in previous collections described as containing the virus, and they support the idea that the human stool is a likely source of the virus.

In order to complete the chain of evidence and prove that flies are capable of acquiring the virus from human excreta, collections were made in Ann Arbor in traps baited with fresh stool from a patient with acute poliomyelitis. The stool was proved to contain the virus by inoculation of a monkey, and flies trapped at the same time but not allowed to feed on the stool were shown to be free of the virus. After separating into species the flies which had fed on the virus-containing stool, seven pools were inoculated intracerebrally in both rhesus and Philippine monkeys and one pool in rhesus monkeys only. One specimen consisting of 183 Phaenicia sericata produced symptoms in both types of monkeys. Another pool of 7 Phormia regina and 1 Callitroga macellaria produced symptoms in a Philippine monkey but none in the rhesus. Two other pools, one containing 13 small feces-inhabiting flies of several species, including Gymnodia arcuata and Myiospila meditabunda, 1 Fannia canicularis, 3 Muscina assimilis and 3 Musca domestica, and the other containing 11 undetermined muscids, 14 Muscina assimilis and Muscina stabulans, 6 Callitroga macellaria and 2 Musca domestica, produced symptoms in rhesus but not in Philippine monkeys. It is interesting that not just one but several species of flies were capable of acquiring the virus, while the house fly was essentially uninvolved. It is also of interest that three pools of flies produced symptoms in rhesus monkeys and that two of these pools did not produce disease in Philippine monkeys. Other workers have clearly expressed the opinion that rhesus monkeys are not susceptible to infection with virus from naturally caught flies.

The evidence clearly demonstrates that the stool of a patient with poliomyelitis can serve as a source of virus for certain flies, which thus become potential vectors of the infectious agent.

Virus was not isolated from normal liver and fruit bait on which the disease-conveying flies subsequently fed, but it is felt that this step in the transmission still offers possibilities which further experimentation should clarify.

It should be added that the virus isolated from flies in this manner has been repeatedly passed in monkeys and has been identified by means of monkey neutralization tests as serologically similar to the Rockford, Ill. (1945) and Minneapolis (1946) strains. It also has a high intracutaneous pathogenicity in monkeys.

SEROLOGIC STUDIES

From time to time the serums of animals associated with the households of patients and having a history of recent illness have been tested for neutralizing antibodies to the mouse-adapted Lansing strain of poliomyelitis virus. Two cows, a rabbit, a horse and several chickens have been found entirely lacking in antibodies.

Forty-six wild rats from epidemic areas of Buffalo and Detroit whose tissues were examined for virus were first bled and their serums tested for Lansing strain neutralizing antibodies.[12] The serums of 45 of these rats showed no evidence of antibodies, but the serum of the remaining rat repeatedly neutralized the Lansing strain of virus. Two other rats were found to maintain circulating antibodies to a strain of Theiler's spontaneous mouse encephalomyelitis virus.

SUMMARY

Attempts to isolate the virus of poliomyelitis from various extrahuman sources in epidemic areas have been made by inoculation of monkeys and of cotton rats and mice.

Thirty-three wild mice, 112 wild rats, 3 muskrats, 4 cats, 1 horse, many chickens, cows and hogs, and 43 pools of insects, 38 of which were flies, representing approximately 15,300 individual specimens, have been so tested.

In addition 24 samples of sewage, 2 of sludge, 1 of soil, 10 of water and 3 of milk have been examined.

The animals, the insects and the other specimens were collected during epidemics of the disease and usually from locations in close proximity of patients.

A mouse-paralyzing agent was isolated from one pool of tissues from wild rats caught in Fort Worth, Texas, in 1943. It has not been identified.

Of 38 pools of flies, one collection of 23 Sarcophaga spp. from rural Tennessee, 1945, was shown to contain poliomyelitis virus.

In all other attempts to isolate the virus the results were negative.

The serums of 2 cows, a horse, a rabbit and 46 wild rats have been tested for neutralizing antibodies to the Lansing strain of virus. All were negative with the exception of that of a wild rat obtained from Detroit in 1944, which had definite virus-neutralizing capacity.

Fly trappings, using fresh normal adult human stool as bait, have shown that certain flies, Phaenicia, Phormia, Sarcophaga, Muscina and Calliphora, are the predominant genera attracted to human feces with the methods of collection used; the common house fly, Musca domestica, is not.

Virus from feces of a patient with poliomyelitis was actually taken up by flies and recovered by inoculation of rhesus monkeys.

ABSTRACT OF DISCUSSION

DR. R. R. SPENCER, Washington, D. C.: This meeting is a high point in the progress of knowledge of viruses. I shall limit my discussion to the possibility that viruses are related

to cancer, presented by Dr. Kidd. The virus field and the cancer field are converging. It is difficult to believe that all types of cancer are due to a single invasive parasitic virus, and discussion is meaningless until more is learned about cells, which are the units of life, and by cells I mean virus particles, as well as body cells. Viruses are rather complex. Certainly, no one has yet grown the mammillary cancer virus; if there be a virus, in tissue culture or in chick embryo, although many of the parasitic viruses have been. Probably it comes down to a question of definition. If you mean by virus, external invasive parasitic organisms, I doubt that mammillary cancers are due to that kind of agent. If, on the other hand, you mean filterable intracellular components, perhaps detached genes or plasmagenes, then each type of cancer may have its own specific kind of intracellular component. There is no clearcut dichotomy anywhere in biology. In other words, there is a gradual change in structure and function all the way from the simplest forms of living things to the most complex, and one should not attempt to make clearcut definitions too quickly. One final point, cancer transplants elicit a rich blood supply and a supporting stroma, as every pathologist knows. They do not, however, elicit a nerve supply. The hyperplasia that results from infection seems to be definitely a defensive mechanism. I do not believe the hyperplasia of cancer is defensive. The body, certainly in the early stages of cancer, does not seem to recognize its presence. I like therefore to think of cancer as an "autoparasite." Regardless of all theories that Dr. Kidd mentioned as to the causation of cancer, and regardless of all the various inciting agents that are known, the end result is always the same. It is one of our own cells that has turned parasite.

Dr. James P. Leake, Washington, D. C.: With reference to Dr. Smadel's paper, I shall make a nonpathologic comment, that for one very important disease, smallpox, the key diagnosis is not in the laboratory but clinical. It must be prompt. Any case of purpura with fever should be considered smallpox as far as precautions are concerned, such as vaccination of those that are in the entourage, until another diagnosis is clear. In the second place, the dependent diagnosis should be made principally not on history, not on the character of the lesions, but on the distribution of the lesions. All of us can be mistaken at times, but it is safer to take precautions.

Dr. E. W. Schultz, Stanford University, Calif.: Little reference has been made to the limitations of specific therapy of virus diseases. It is important to remember in this connection that antibodies are much too large to enter cells and that there is little reason to expect therapeutic effects with immune serums after the invasion of susceptible cells has occurred. The same applies in general to chemotherapy. It would appear that future attempts to control these diseases will have to center largely around possible means of modifying the native susceptibility of vulnerable cells or preventing their initial invasion by the timely use of prophylactic agents. Virus diseases, more than any other group of diseases, depend on prophylactic measures for their control. Once infection has occurred the disease is largely out of control.

Dr. J. E. Smadel, Washington, D. C.: Viruses differ from one another. Nevertheless, all viruses have certain biologic properties in common, since they are obligate intracellular parasitic microbes. There is a tendency to think that the similarities in basic biologic properties extend to close similarities in physical, chemical and immunologic properties. The fallacy of this generalization has been touched on but not emphasized. The electron micrographs of Dr. Wyckoff do not bring out these differences in viruses as well as do other methods. Thus, certain of the plant viruses have a relatively simple chemical structure, being composed solely of nucleoprotein, which behaves as a single antigenic substance. On the other hand, the large virus of vaccinia contains protein, nucleoprotein, carbohydrate, lipid and minerals; in fact, it has the biochemical characteristics of bacteria or protoplasm. The complexity of this virus is further indicated by the fact that it contains at least five different antigenic structures. These viruses represent the two ends of the spectrum, agents in between show varying grades of similarity to the end viruses. I wish to reiterate the heresy which I mentioned earlier—don't ask for isolations. The Army has had greater experience in attempts at isolation of viruses than any other group in the United States. We consider it relatively unprofitable for the routine diagnosis of virus and rickettsial disease.

TRANSURETHRAL RESECTION FOR VESICAL DYSFUNCTION IN CASES OF TABES DORSALIS

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In 1941, we reported the results of a study of vesical dysfunction in cases of tabes dorsalis and analyzed the results of transurethral resection in 35 of the cases.[1] In these cases, the results of transurethral resection were very good. We recently have made a follow-up study of these 35 cases and of 44 additional cases of tabes dorsalis in which transurethral resection has been performed since Dec. 31, 1940. These two groups of cases form the basis of the present report.

In making such a study, it must be emphasized that it is impossible in every case to distinguish accurately vesical dysfunction caused by the tabetic state alone from that which results from hypertrophy of the prostate gland or other obstruction of the vesical neck in a case in which tabes dorsalis is only a coincidental finding and of no urologic importance. It is true that the extremes of these conditions are rather easily recognized, but intermediate conditions may be difficult to classify. The chief reason for this difficulty lies in the basic neuromechanics and obstructive factors involved in the disability. The neurophysiology of normal micturition has been described elsewhere,[2] and it is so well known that description here seems unnecessary. The tabetic process damages the posterior spinal ganglions, the posterior sensory roots and the posterior sensory columns of the spinal cord. This may block not only the impulses which pass through the sensory component of the simple spinal reflex arc and which control micturition (the level of which is in the sacral portion of the cord) but also may block the impulses which pass through the sensory part of the suprasegmental conditioning reflex and mediate vesical control by means of subconscious or conscious inhibitory impulses from the higher levels. With involvement of the sensory component of the lower reflex arc, it is apparent that more and stronger impulses would be necessary to incite reflex vesical contraction. This would result in progressive vesical distention, loss of tone and atony. Damage to the sensory component of the suprasegmental conditioning reflex would interfere with the stimuli which incite the proper flow of inhibitory impulses down the corticospinal tracts to supply subconscious and voluntary control of the lower reflex arc for micturition. In other words, the patient might not experience the desire to micturate until greater and greater distention of the bladder occurs, and the micturition could begin without the patient's being aware of it.

It is easy to visualize how such a lesion can give rise to urinary retention and incontinence. The bladder

From the Section on Urology, Mayo Clinic (Dr. Emmett) and the Mayo Foundation (Dr. Beare, Fellow in Urology).

1. Emmett, J. L., and Beare, J. B.: Bladder Difficulties of Tabetic Patients with Special Reference to Treatment by Transurethral Resection, J. A. M. A. **117**: 1930-1934 (Dec. 6) 1941.

2. Emmett, J. L., and Dunn, J. H.: Transurethral Resection in the Surgical Management of Cord Bladder, Surg., Gynec. & Obst. **83**: 597-612 (Nov.) 1946.

becomes increasingly stretched, loses its tone and becomes atonic. There results an imbalance between the detrusor urinae muscle and the vesical neck,[3] which results in residual urine and retention. Under such circumstances, even a normal-appearing vesical neck may be obstructive. Any obstruction of the vesical neck, even of a minimal degree, may increase the imbalance, and the fact that most patients who have tabes dorsalis are more than 40 years of age stipulates that almost all men who have this disease have some degree of prostatic hyperplasia, although it may be of mild degree.

Our experience with this problem has left us with the impression that most of the urinary incontinence in tabetic patients may be explained in two ways: (1) overflow from a distended bladder and (2) involuntary micturition caused by reflex emptying of the bladder not properly controlled by the suprasegmental conditioning reflex, the sensory components of which have been damaged. To put it simply, since the patient is not aware that micturition is about to occur, sufficient inhibitory impulses are not sent down from the conscious or subconscious level to prevent it.

It is apparent, therefore, that the over-all problem of vesical dysfunction in tabetic patients is composed of three rather ill defined parts; namely, (1) vesical dysfunction arising primarily from the neurogenic lesion caused by the tabetic state, (2) obstruction of the vesical neck in a case in which tabes dorsalis is only a coincidental finding and plays no part in the vesical dysfunction and (3) a combination of both factors. It is our feeling that most instances of vesical dysfunction belong in the last group.

In our previous article [1] on this subject, we analyzed the results in 35 cases of tabes dorsalis in which transurethral resection had been performed. It was apparent from this study that both residual urine and urinary incontinence could be eliminated in almost all cases. It was thoroughly demonstrated that prostatic operation could be done with no more concern or fear of postoperative incontinence in the tabetic patient than in the nontabetic patient. It also was observed in this series of cases that the amount of tissue removed was not great; it was less than 5 Gm. in many cases. This observation further emphasized that minimal amounts of obstruction at the vesical neck can produce vesical decompensation in the weakened tabetic bladder.

Inasmuch as minimal degrees of obstruction of the vesical neck or even a normal-appearing vesical neck can be the precipitating factor in vesical dysfunction in cases of tabes dorsalis, one might logically reason that minimal degrees of postoperative scarring or contraction of the vesical neck occurring after transurethral resection could cause sufficient obstruction to produce a recurrence of the vesical dysfunction and residual urine. In such an event, it could also be assumed that transurethral removal of the postoperative scar tissue or removal of a recurring adenoma might again yield a good result. In short, we have wondered whether any of the 35 patients who were operated on prior to Jan. 1, 1941, have had to undergo further treatment because of a recurrence of their former symptoms. To investigate this problem we have reviewed all of these cases. In all of these cases, more than six years have elapsed since transurethral resection first was performed at the Mayo Clinic. One of the patients has returned to the clinic for further treatment. Letters of inquiry were sent to all of the other patients, and thirty-one replies were received. Follow-up data, therefore, are available in 32 of the 35 cases. In 16 of the 32 cases, the patients were alive at the time of inquiry. In 9 of these 16 cases, the letters indicated that the patients did not have any symptoms referable to the urinary bladder; there was no urinary frequency or incontinence. In 6 other cases, the patients reported that their vesical function was satisfactory except for the presence of varying degrees of urinary frequency and some nocturia. All of the 15 patients felt that they were emptying their bladders completely, although some stated that the urinary stream was not so large as it had been immediately after the transurethral resection. (This would indicate that these patients have had a slight degree of postoperative contracture or scarring of the vesical neck.) In the letters of inquiry, we requested the patients to have a determination of the amount of residual urine made, if possible. All of the 6 patients who complied with this request reported that they were emptying their bladders completely.

The case in which the patient returned to the clinic because of a recurrence of his former symptoms is of sufficient interest to be presented here in abstract form, as it is illustrative of the general problem.

A man aged 42 years first came to the clinic in December 1918. His chief complaint was difficulty with his urinary bladder, which consisted of nocturnal incontinence, a diurnal urgency type of incontinence and difficulty in initiating and maintaining the urinary stream. In addition, he complained of loss of sexual power, an unsteady gait (especially at night) and weakness of his legs. He stated that he had had a penile chancre at the age of 21 years.

Examination disclosed tabes dorsalis. The Wassermann reaction on the serum and cerebrospinal fluid was positive. Romberg's sign was present. Urologic examination disclosed the presence of 400 cc. of infected residual urine. Cystoscopy revealed a large atonic bladder with little if any trabeculation. The diagnosis was tabetic cord bladder. The patient was advised to employ periodic vesical lavage.

The patient returned to the clinic twenty-one years later; that is, in June 1939. His chief reason for seeking medical aid at this time was urinary incontinence and foul-smelling urine that made it impossible for him to live in normal society. He also complained of "lightning" pains around the abdomen. Vesical lavage had produced some relief of the urinary symptoms for several years, but in the past two or three years the incontinence had become so great that he had been forced to wear a rubber urinal.

Neurologic examination revealed the same signs of tabes dorsalis that had been noted at his examination twenty-one years previously. The bladder contained 1,000 cc. of foul, infected, residual urine. Cystoscopy disclosed a large atonic bladder with minimal trabeculation. The prostatic urethra and vesical neck appeared to be relaxed, dilated and "pulled open" as a result of the vesical distention. There was adenomatous enlargement, grade 1, of all three lobes of the prostate gland. The diagnosis was tabetic cord bladder associated with minimal prostatic hyperplasia.

A transurethral resection was performed on June 30, 1939, with the Thompson cold punch resectoscope. The removal of 8 Gm. of tissue seemed to open the prostatic urethra widely. Pathologic examination of the excised tissue revealed adenofibromatous hyperplasia. The patient was able to empty his bladder completely, although it was necessary for him to use considerable abdominal straining. Several minutes were required to empty the bladder completely. The urinary incontinence was relieved entirely. Owing to the sensory involvement, he never regained the desire to micturate; he therefore was instructed to micturate every three hours. The urinary infection was eliminated and the patient was dismissed from our care.

3. Emmett, J. L.: Urinary Retention from Imbalance of Detrusor and Vesical Neck: Treatment by Transurethral Resection, J. Urol. 43: 692-704 (May) 1940.

His next visit to the clinic was seven years later; that is, in June 1946, when he was 70 years of age. He stated that his urinary function had been satisfactory for about five years after the last transurethral resection. In the two years before he returned to the clinic, previous symptoms had returned gradually. He again complained of urinary incontinence and infected urine. Urologic examination revealed that his bladder contained 600 cc. of residual urine. Cystoscopy revealed a moderate degree of postoperative contracture of the vesical neck and some residual or recurrent adenomatous hyperplasia in both lateral lobes of the prostate gland, near the apex of the gland. The bladder was large and atonic.

Transurethral resection was performed on June 11, 1946. As the resection proceeded, it became apparent that there was a substantial amount of adenomatous tissue at the apex of the prostate gland. Twelve grams of tissue was removed. Examination of the excised tissue disclosed adenofibromatous hyperplasia. The result was excellent; the patient was able to empty the bladder completely with a good stream. It was still necessary for him to use abdominal straining and he was advised, as he had been after the previous operation, to empty his bladder regularly every three or four hours.

ANALYSIS OF FORTY-FOUR CASES OF TABES DORSALIS IN WHICH TRANSURETHRAL RESECTION WAS PERFORMED

We have been interested to know whether our results with transurethral resection in tabetic patients will continue to be as favorable as indicated in our previous report. Accordingly, we have made a study of 44 cases of tabes dorsalis in which transurethral resection was performed at the clinic in the years 1941 to 1945, inclusive. As mentioned in our original article, we feel that it is impossible to determine with any degree of accuracy in every case the proportion of the vesical dysfunction caused by the primary neurogenic atony and that produced by obstruction of the vesical neck. In most cases there was no question but that the tabetic condition was the predominating factor; in other cases, it seemed definite that the predominating factor was obstruction at the vesical neck. It is entirely possible that in a few cases the tabes dorsalis was only a coincidental finding and did not contribute to the vesical dysfunction. In the absence of an accurate method of distinguishing these conditions, it seems best to consider them as a single group.

Age and Sex.—Of the 44 patients, 43 were men and 1 was a woman. All except 4 were 50 or more years of age (table 1), which substantiates the thesis that most of the patients are in the age of prostatism when the vesical symptoms become sufficiently disturbing to require medical care.

TABLE 1.—*Age of Patients in Forty-Four Cases of Tabes Dorsalis in Which Transurethral Resection Was Performed*

Age, Years	Cases
40 to 49	4
50 to 59	18
60 to 69	16
70 to 79	6

Urinary Incontinence and Residual Urine.—Seventeen of the 44 patients complained of some type of "incontinence." In 6 cases, the incontinence was nocturnal only and in 1 case it was of a precipitate urgency type. In the remaining 10 cases, the urinary leakage occurred during both the day and night and varied in degree from a mild type consisting of an occasional involuntary spurt of urine to a more or less continual overflow type of dribbling from a distended bladder. In all except 1 case, the bladder contained more than 200 cc. of residual urine; in 12 of the cases, more than 300 cc. of residual urine was present. The largest amount found in any of these 17 cases was 1,200 cc. The amount of residual urine present in the entire group of 44 cases is shown in table 2.

TABLE 2.—*Amount of Residual Urine Before Transurethral Resection in Forty-Four Cases of Tabes Dorsalis*

Residual Urine, Cc.	Cases	
	Number	Percentage
More than 500	8	18
100 to 500	22	50
Less than 100	14	32

Type of Obstruction of the Vesical Neck.—Consistent with our previous experience, the degree of obstruction at the vesical neck was not great. Contractures of the vesical neck, small adenomatous collars and a small degree of hypertrophy of the lateral and median lobes predominated. It should be pointed out that in many of the cases cystoscopy suggested that the vesical neck was relaxed and dilated and was probably not causing any obstruction. This appearance is due to the distended bladder, which has pulled open and stretched the vesical neck. (The surgeon should not let this condition deter him from performing a transurethral resection, as the results of transurethral resection in this type of case are as good as in any other.) In the majority of cases, it was necessary to remove less than 10 Gm. of tissue (table 3), while in only 9 cases was it necessary to remove more than 20 Gm.

TABLE 3.—*Weight and Type of Tissue Removed by Transurethral Resection in Forty-Four Cases of Tabes Dorsalis*

Weight of Tissue, Gm.	Cases	Type of Tissue		
		Adenofibromatous Hyperplasia	Carcinoma	Inflamed Smooth Muscle
0 to 3	2	1	..	1
4 to 5	5	4	..	1
6 to 10	18	17	..	1
11 to 20	10	10	..	..
21 to 50	9	7	2	..
Total	44	39	2	3

of tissue. In some cases, it was difficult to demonstrate obstruction at the vesical neck until resection actually was begun.

Results.—The results of transurethral resection were most satisfactory and essentially paralleled those obtained in our previous series. The results were classed as good in 39 cases and as fair in 3 cases. Two patients were unimproved. By the term "good," we mean that the patient is able to void with a good stream, can empty the bladder completely and has no urinary incontinence.

Of the 17 patients who complained of urinary incontinence prior to operation, 15 secured excellent results and complete relief of the incontinence. One patient, although able to empty his bladder completely, continued to have a moderate degree of urinary urgency while the remaining patient still complains of nocturnal enuresis and of difficulty in expelling his urine.

Reviewing the 5 cases in which the results were not entirely satisfactory, one gains the impression that further cystoscopy is indicated and that in some of the

cases removal of additional tissue would improve the vesical function. In such cases, it often requires careful observation and judgment to recognize and remove minimal amounts of tissue from the vesical neck. Removal of such tissue may make the difference between an excellent and an unsatisfactory result.

TRANSURETHRAL RESECTION IN TABETIC WOMEN

In our previous study, it was pointed out that in cases of tabes dorsalis vesical dysfunction is much more common among men than women. This is no doubt explained by the fact that obstruction of the vesical neck is so much more common in men than it is in women. Nevertheless, vesical dysfunction with residual urine and urinary incontinence does occur in women. This condition can also be cared for by transurethral resection. The following case is illustrative of the condition.

A woman aged 62 years came to the clinic on Oct. 22, 1945. She complained of a girdle type of pain which encircled the left side of the thorax at the level of the angle of the scapula. The pain had been present intermittently for several years. It recently had become so severe that morphine had been necessary for relief. She also complained of having "lost control of her bladder." This had consisted chiefly of nocturnal incontinence; however, it recently had begun to be troublesome during the day. The amount of urine that was expelled in this manner was sufficient to wet her clothes.

Her past history suggested that she probably had had a chancre at the age of 19 years and that the lesion never had been treated. For many years, she had "prided herself" on the length of time she could go without voiding. More recently, she had experienced moderate difficulty in initiating the urinary stream; recently, incontinence had developed and had become annoying.

Neurologic examination revealed typical signs of tabes dorsalis. The Wassermann reaction and results of flocculation tests on the blood and cerebrospinal fluid were strongly positive, and examination of the spinal fluid revealed a paretic colloidal gold curve. The girdle pain was interpreted as being due to a typical tabetic crisis.

Urologic examination revealed 350 cc. of residual urine. Cystoscopy revealed a large atonic bladder and trabeculation, grade 1. The urethra was very short. The vesical neck did not appear to be causing a great deal of obstruction. An excretory urogram did not disclose any abnormality of the kidneys. The diagnosis was tabetic cord bladder.

Transurethral resection was performed on Nov. 26, 1945, by means of the small punch resectoscope. Fifteen pieces of tissue were removed from the entire circumference of the vesical neck. The results of the operation were excellent. When the catheter was removed, the patient was able to void well with a good stream and could empty her bladder completely. The diurnal and nocturnal incontineuce were completely eliminated. On her dismissal, the patient was instructed to micturate regularly at least every three hours.

COMMENT

It is our opinion that vesical dysfunction associated with tabes dorsalis is no longer a therapeutic problem of any importance, since consistently good results may be obtained by means of transurethral resection of the vesical neck. The explanation of how transurethral resection corrects vesical dysfunction in this disease seems relatively simple, although it must be admitted that some points are more or less theoretic. The elimination of residual urine is brought about by weakening the vesical neck sufficiently to permit the weakened atonic bladder, aided by intra-abdominal and, if necessary, manual compression, to expel the urine completely. The elimination of the residual urine also relieves the incontinence in cases in which the patients are suffering from an overflow type of incontinence. The explanation of the relief of incontinence that is principally an involuntary type of micturition also seems fairly simple. The elimination of residual urine increases the reservoir capacity of the bladder. The patient is instructed to micturate regularly every three or four hours to prevent undue distention of the bladder so that the chance of involuntary micturition is minimized. He is instructed to take the time and make the effort to empty his bladder completely at each micturition. In some cases in which advanced sensory damage is present, the patients never may regain the desire to micturate. Such patients must be carefully taught to micturate at regular intervals and not to wait for the desire to micturate. Inasmuch as the bladder is emptied completely at each voiding, the urine may be kept free of infection; therefore, for all practical purposes, the vesical function may be considered normal.

One word of caution should be given. Inasmuch as small degrees of obstruction of the vesical neck can precipitate vesical dysfunction in cases of tabes dorsalis, small degrees of postoperative contracture may conceivably cause a recurrence of the obstruction. Because of this, such patients should be reexamined at yearly intervals to determine whether any residual urine is present. If it is, cystoscopic reexamination of the vesical neck should be performed and any scar tissue should be excised.

POLYMYXIN

A Note on Experimental and Clinical Investigations

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In May 1947, Benedict and Langlykke [1] reported that sterile culture filtrates of Bacillus polymyxa in dilutions of 1:1,000 inhibited the growth of Brucella bronchiseptica in culture. Shortly after this report, Stansly, Shepherd and White [2] independently described the isolation of an antibiotic substance from B. polymyxa which they named "polymyxin." This antibiotic was shown by them to be effective only against gram-negative organisms in vitro, and to possess a high degree of therapeutic activity against experimental infections produced in mice by the inoculation of Klebsiella pneumoniae or Pasteurella multocida. It was also effective against experimental fowl typhoid infections in chicks. Subsequently, Stansly and Schlosser [3] established the identity of polymyxin as a new antibiotic and developed a method for its bio-assay. Not long after the two original reports on this antibiotic appeared, Ainsworth, Brown and Brownlee [4] announced that they had isolated an antibiotic, active against gram-negative organisms, from cultures of Bacillus aerosporus Greer. To this agent they gave the name

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The polymyxin was furnished by the Lederle Laboratories Division, American Cyanamid Company.

1. Benedict, R. G., and Langlykke, A. F.: J. Bact. 54: 24 (July) 1947.

2. Stansly, P. G.; Shepherd, R. D., and White, H. J.: Bull. Johns Hopkins Hosp. 81: 43 (July) 1947.

3. Stansly, P. G., and Schlosser, M. E.: J. Bact. 54: 549 and 585 (Nov.) 1947.

4. Ainsworth, G. C.; Brown, A. M., and Brownlee, G.: Nature, London 160: 263 (Aug. 23) 1947.

"aerosporin." Recently, Brownlee and Bushby [5] have described in detail the bactericidal, toxicologic and pharmacologic properties, and experimental therapeutic effectiveness of aerosporin, while Swift [6] has reported that this antibotic is of some value in the treatment of whooping cough in children. Although polymyxin and aerosporin are derived from similar micro-organisms, recent comparisons of the two products suggest that they are dissimilar in chemical composition. [7]

We wish to report briefly upon the experimental and clinical observations which we have made during the past six months with polymyxin (hydrochloride). This antibiotic in vitro is most effective in an acid medium, is relatively heat stable and loses little of its activity in the presence of serum. The strains of Escherichia coli, Aerobacter aerogenes and K. pneumoniae which have been tested are susceptible to 0.3 microgram of polymyxin per cubic centimeter when an inoculum of 200,000 bacilli is used. Pseudomonas aeruginosa is slightly more resistant to this antibiotic, while the strains of P. vulgaris and N. intracellularis so far tested in vitro appear to be completely resistant. Polymyxin in its effective concentrations appears to be bactericidal in its action on susceptible micro-organisms. Like Stansly et al. [2], we have found it was impossible to produce resistant strains from susceptible organisms in vitro.

The acute toxicity of polymyxin was determined in mice by single subcutaneous injections and the LD 50 was found to be 50 to 300 mg. per kilogram. While dogs survived single intravaneous injections of 10 to 15 mg. per kilogram of body weight, single intravenous injections of 25 mg. per kilogram produced death. Dogs tolerated 5 and 10 mg. of the antibiotic per kilogram when given injections twice daily by the intramuscular route for seven days. Intrathecal injections of 1 and 5 mg. of the drug in dogs produced no untoward reactions, while 10 mg. produced transient paresis of the hind legs.

Ninety minutes after dogs had received single intramuscular doses of 5 and 10 mg. per kilogram, serum concentrations of 2.5 and 5.0 micrograms of polymyxin per cubic centimeter were recorded. Three and one-half hours after these doses, serum concentrations of 2.5 and 1.25 micrograms per cubic centimeter were noted. When dogs were given 5 and 10 mg. of the compound per kilogram twice daily for seven days, serum concentrations of 10 to 20 micrograms of polymyxin per cubic centimeter were observed. The antibiotic was not detected in the spinal fluid of dogs in which high serum concentrations of polymyxin were present. When polymyxin was administered to human beings in divided doses by the intramuscular route at intervals of three hours in amounts not to exceed a total daily dose of 3 mg. per kilogram of body weight, concentrations of 0.6 to 1.3 micrograms per cubic centimeter were noted in the serum after twenty-four hours of therapy. Detectable amounts of polymyxin began to appear in the urine twelve hours after the initiation of the dosage schedule just described. After twenty-four hours of its administration, effective bactericidal concentrations of the antibiotic were found in the urine. In 1 person, suffering from purulent meningitis and treated with polymyxin, none of the agent was detected in the spinal fluid.

As is shown in the table, single doses of 1 mg. of polymyxin per kilogram of body weight administered by the subcutaneous route protected the majority of mice which had been previously infected by the inoculation of 1,000 minimum lethal doses of either K. pneumoniae (type A) or Hemophelus influenzae (type B) by the intraperitoneal route. These results confirmed previous observations on the therapeutic effectiveness of this antibiotic in experimental gram-negative infections. [2] Comparable experimental infections treated with streptomycin in doses of 1 or 5 mg. per kilogram of body weight were used as therapeutic controls. Under the conditions of the test, polymyxin appeared to be five to ten times more effective in the control of these experimental infections than was streptomycin. Furthermore, it has been noted that while neither a bacteriostatic nor bactericidal effect could be demonstrated against Neisseria intracellularis in vitro, polymyxin had a definite curative effect in experimental meningococcic infections in mice. This paradox is being investigated.

TABLE 1.—*Comparison Of Streptomycin and Polymyxin*

Drug	Dose, Single (Subcutaneously) Mg./Kg.	Inoculum*	Deaths on Day Indicated						Survivals After Six Days	
			1	2	3	4	5	6	Number	Percentage Total
Control	—	K. pneumoniae† Type A	10	–	–	–	–	–	0	0.0
Streptomycin	1	K. pneumoniae Type A†	1	4	9	1	–	–	5	25.0
	5		–	–	3	–	–	–	7	70.0
Polymyxin	1	K. pneumoniae Type A†	–	–	1	2	–	–	17	85.0
	5		–	–	–	–	–	–	20	100.0
Control	—	H. influenzae Type B‡	9	–	–	–	–	–	1	10.0
Streptomycin	1	H. influenzae Type B‡	16	–	–	–	–	–	4	20.0
	5		2	–	–	–	–	1	7	70.0
Polymyxin	1	H. influenzae Type B‡	–	1	–	–	–	–	19	95.0
	5		–	–	–	–	–	–	20	100.0

*In all instances 1,000 lethal doses were given.
†K. pneumoniae, type A, was injected intraperitoneally.
‡H. influenzae, type B, was injected intraperitoneally in 5 per cent hog gastric mucin.

Polymyxin in total daily dosages of up to 5 mg. per kilogram of body weight, given in a special buffer solution (*pH* 7.4) at intervals of three hours has been used to treat patients seriously ill with infections due to Pseudonionas aeruginosa, K. pneumoniae, Hemophilus pertussis, and Brucella abortus. To date, the results have been such as to demonstrate clearly that polymyxin has a therapeutic effect against infections produced by these organisms in human beings. Too few patients have been treated to make any definite statements in regard to the clinical toxicity of polymyxin. One instance of fever, possibly due to the drug, has been noted. Other toxic reactions undoubtedly will occur.

CONCLUSION

Polymyxin is a new antibiotic uniquely and highly active in vitro against certain varieties of gram-negative micro-organisms. Its acute toxicity in experimental animals is considerably greater than that of penicillin or streptomycin. After intramuscular injection of the antibiotic, it promptly enters the blood stream, but it does not pass the blood-brain barrier. It is excreted slowly in the urine.

In certain experimental infections produced by the inoculation of gram-negative organisms in mice, polymyxin appears to be definitely more effective than streptomycin. The results following its use in certain types of

5. Brownlee, G., and Bushby, S. R. M.: Lancet 1948 1: 127 (Jan. 24) 1948.
6. Swift, N. P.: Lancet 1: 133 (Jan. 24) 1948.
7. Subbarow, Y.: Personal communications to the authors.

clinical infections produced by gram-negative bacilli are interesting. However, careful clinical trials of this compound in selected and suitable types of infections must be made before the therapeutic effects of polymyxin can be evaluated.

Clinical Notes, Suggestions and New Instruments

DEVELOPMENT OF APLASTIC ANEMIA DURING THE USE OF STREPTOMYCIN

Report of Two Cases

CAPTAIN V. F. DEYKE, and
LIEUTENANT COLONEL J. B. WALLACE,
Medical Corps, United States Army

CASE 1.—A white man aged 46 with moderately advanced pulmonary tuberculosis, was admitted to Fitzsimons General Hospital in January 1947. On April 1 the patient was started on 2 Gm. of streptomycin daily, intramuscularly in five equally divided doses. There was no history of blood disorder or any evidence of such on periodic examinations until June 19, at which time the erythrocyte count was 3,100,000, the leukocyte count was 3,500, neutrophils 54 per cent and lymphocytes 46 per cent. Streptomycin was discontinued on that date. On June 29 the leukocyte count was 2,000 with 91 per cent lymphocytes. The platelets were markedly decreased. On that date, the usual vigorous measures were begun to combat aplastic anemia. In spite of this the blood picture continued to deteriorate until July 7, when the erythrocyte count was 2,800,000. The leukocytes measured 800, of which 2 per cent were neutrophils and 98 per cent lymphocytes. No platelets were seen. The patient died July 8, nineteen days later. Autopsy revealed pronounced hypoplasia of bone marrow. The proximal end of the femur was filled with a soft yellow fatty material. A similar change was noted in the rib bone marrow. Microscopically the marrow was predominantly replaced by fat, with scattered occasional islands of hemopoietic tissue.

CASE 2.—A white man aged 27 with active moderately advanced tuberculosis was admitted to the hospital Feb. 5, 1947 with a history suggesting onset of illness two months previously. On March 17 he was started on 2 Gm. of streptomycin daily administered intramuscularly in five equally divided doses. Periodic blood counts revealed no abnormality until June 20, when a depression of all blood elements was noted. Streptomycin therapy was discontinued immediately, and the usual vigorous efforts were made to combat aplastic anemia. The blood picture has deteriorated to this writing (July 17) when the red blood cell count is 1,400,000, the white blood cell count 1,100, neutrophils 1 per cent and lymphocytes 99 per cent; no platelets are seen. Repeated sternal marrow examinations reveal a decided diminution in the number of the young red and granulocytic series. Recovery is doubtful.

COMMENT

Some 400 patients have been, or are being, treated with streptomycin to date at this hospital. In 2 patients from this number a serious depression of blood elements developed during streptomycin therapy, beginning on the seventy-ninth and ninety-fifth days of treatment. Neither patient appeared to have disseminated hematogenous tuberculosis. One patient had received an occasional "seconal sodium" tablet and the other patient had received some diphenhydramine hydrochloride. It is our opinion that neither of these drugs was the causative agent.

Review of the literature indicates that of some 900 patients, other than the series at the Fitzsimons General Hospital, treated with streptomycin, 8 have shown a relatively mild leukopenia, 6 of whom had a relative neutropenia. These were self limiting. There is reported 1 case of agranulocytosis, but no mention is made as to its severity and outcome.[1]

From Fitzsimons General Hospital.

1. Farrington, et al. Streptomycin Toxicity, J. A. M. A. **134**: 679-688 (June 21) 1947. A Preliminary Statement Concerning the Effects of Streptomycin Upon Tuberculosis in Man, manuscript prepared by the Surgeons General of the Army, Navy, and Veterans' Administration, July 3, 1947

Council on Physical Medicine

The following article has been adopted by the Council on Physical Medicine.

The Council wishes to express its appreciation for the valuable cooperation of the Consultants on Ophthalmic Devices in reviewing and adopting this article. The consultants are Drs. Walter B. Lancaster, chairman; Thomas D. Allen, S. Judd Beach, Conrad Berens, Frederick C. Cordes, Alfred Cowan, William H. Luedde, Lawrence T. Post, Avery D. Prangen and Kenneth C. Swan.

HOWARD A. CARTER, Secretary.

TINTED LENSES

ALFRED COWAN, M.D.
Philadelphia

The following statement is made for the benefit of the public and for those ophthalmologists who are insufficiently informed and therefore misled by the extravagant and often untrue claims of a number of manufacturers of trademarked tinted lenses.

The vogue for tinted lenses has reached such an extent that most laymen and many ophthalmologists believe that the eyes need protection not only against daylight but against any light, even night light. Informed ophthalmologists disapprove the widespread, continuous and indiscriminate use of tinted lenses and object to the methods and wording of the advertisers of these glasses.

The purpose of light-filtering glasses is to protect the eyes against painful or harmful light. Unless the eyes are sick or abnormally sensitive, dark glasses are indicated only in the presence of extraordinary, excessive or misdirected light. Healthy, properly corrected eyes should be well able to tolerate bright sunlight unless it is reflected directly into the eyes by water, snow, sand or the like. The sole purpose of so-called "sun glasses" is to reduce considerably the amount of direct or reflected sunlight on those occasions when the amount is so great that it interferes with vision. On the occasions when protection is necessary the glasses should be dark enough to absorb from 60 to 75 per cent of the light and they should be colorless—smoke or gray.

Any person with normally healthy eyes should be comfortable under ordinary bright sunlight. Those who would be annoyed by less than unusually brilliant sunlight should be rare exceptions, not the rule.

Tinted lenses should not be worn indoors under properly placed artificial light and never outdoors at night. They are dangerous for night driving; the glare of an automobile headlight is due to the contrast with the surrounding darkness, and no type of tinted glass can change that. The sense of ocular fatigue after day driving is more often due to uncorrected or improperly corrected errors of refraction or of muscle balance than to the bright light.

Despite the fantastic, absurd and untrue claims of the manufacturers of certain tinted glasses, the lighter shades of colored glass—tints that are hardly perceptible—offer little more protection against glare than clear glass. Nevertheless, promoters assert that through their miracle glasses the light is soft, cool and restful, as in a cathedral; work, they claim, is done more efficiently and with greater comfort. These hyperphysical lenses are said to match the complexion; to be inconspicuous yet improve the appearance; even to increase the visual acuity somehow or other; to protect the eyes against the ultraviolet and infrared in daylight, against amounts of energy which no one except the exploiters of these glasses would ever consider harmful; to keep out most of the light which seems to be bad light and let in only the good light. Through these glasses they claim, there are no annoying color disturbances—the makers have produced the impossible, a colored glass without selectivity. They show pictures of persons reading through their wonderful lenses by the light of a lamp in an otherwise dark room—a spotlight; suggesting that inadequate or poorly distributed artificial light is all right if you wear the right tint.

The exploiters of these glasses would have the ophthalmologist consider a tint as a component of every lens he prescribes. This means that for the "visual comfort" of his patient the ophthalmologist would have to order a different shade for every intensity of light indoors and out. The patient would need a photometer and a bag full of tinted spectacles to meet what they suggest as requirements for proper vision.

AUREX HEARING AID, MODEL H, ACCEPTABLE

Manufacturer: Aurex Corporation, 1117 North Franklin Street, Chicago 10.

This is a plastic cased hearing aid, with separate batteries. The crystal receiver supplied has the Aurex trademark and is connected to the amplifier by a plastic covered cord (plugs at both ends). A four conductor battery cord connects to the batteries used.

Aurex hearing aid, model H.

One sliding type control on the side of the case serves as the switch and volume control. A rotating fan-type shutter may be turned from the center front of the case to close the microphone openings and serves as a partial tone control.

Dimensions and Weight

Dimensions: 70 by 63 by 22 mm. (2¾ by 2½ by ⅞ inch).

Weight: Unit alone, approximately 92 Gm. (3¼ ounces). With batteries, approximately 269 Gm. (9½ ounces).

Battery data		Voltage	Current
A 1½ volts	.....	1.4 volts	55.0 milliamperes
B 30 volts	(Quiet).....	29 volts	0.6 milliampere
	(Squealing)..	29 volts	1.0 milliampere

Acoustical Gain

Measurements were made of the acoustical gain of the instrument in decibels. This is the decibel difference in sound pressure between the pressure at the face of the microphone opening (with the instrument set in a 16 by 8 inch, 40.6 by 20.3 cm., baffle) and the sound pressure produced by the receiver in a 2 cc. coupler. The microphone sound pressure was held at a level of 40 decibels over 0.0002 dyne per square centimeter. Typical results, obtained with the volume control full on and the tone control shutter open, are here tabulated for seven frequencies.

Frequency (cycles)	256	512	1,024	1,200	2,250	3,100	4,096
Gain in decibels	53	56	69	63	55	34	42

Maximum Output Pressure

Measurements were made of the approximate maximum sound pressure the instrument would produce in the 2 cc. coupler with the instrument set for full gain and shutter open. Levels are in decibels relative to 0.0002 dyne per square centimeter.

Frequency	Input Level	Maximum Output Level
600 cycles	55 decibels	103 decibels
1,024 cycles	55 decibels	113 decibels
2,048 cycles	60 decibels	104 decibels

Intelligibility Tests

Intelligibility tests (random words) were made with a person of normal hearing seated inside a booth giving about 30 decibels sound reduction. The speaking person was outside the booth using a normal tone of voice. The score made under these critical conditions was 48 per cent. These conditions are severer than tests using a deafened observer, because any internal instrument noise causes a lower signal to noise ratio due to the lower threshold of the person with normal hearing.

The Council on Physical Medicine voted to include the Aurex Hearing Aid, Model H, in the list of accepted devices.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

ISOBORNYL THIOCYANOACETATE-TECHNICAL.—$C_{13}H_{19}N_2OS$.—M. W. 253.35. The technical grade of isobornyl thiocyanoacetate contains 82 per cent or more of isobornyl thiocyanoacetate with other terpenes.

Actions and Uses.—Isobornyl thiocyanoacetate is one of the thiocyanates shown to be effective as a pediculicide. A mixture of the technical grade of this compound with dioctyl sodium sulfosuccinate in the form of an oil emulsion is useful for external application to eradicate both the adult and ova forms of Phthirius pubis, Pediculus humanus capitis and Pediculus humanus corporis. Skin irritation studies reveal that the compound may act as a mild primary irritant to the skin of some persons, but there is no evidence that it acts as a sensitizing agent. It should not be applied too close to the eyes or to mucous membranes.

Dosage.—An oil emulsion containing isobornyl thiocyanoacetate—technical 5 per cent dioctyl sodium sulfosuccinate 0.6 per cent is applied externally in amounts of 30 to 60 cc. depending on the site involved (quantity of hair), worked into a lather and allowed to remain for from five to ten minutes. In the case of the scalp, the hair is then combed and permitted to dry, and the emulsion is left on over night. The head is washed the following day. In the case of the pubis and other regions of the body, the emulsion is worked into a lather and then washed off with soap and water. Care must be taken that the emulsion does not remain in contact with the skin for too long. More than two such applications should be avoided.

Tests and Standards.—

Isobornyl thiocyanoacetate-technical occurs as a yellow, oily liquid, possessing a terpene-like odor. It is very soluble in alcohol, benzene, chloroform and ether; it is practically insoluble in water. The refractive index of isobornyl thiocyanoacetate-technical is 1.512. Its specific gravity at 25 C. is 1.1465. The acid number is 1.19.

Add to about 25 mg. of isobornyl thiocyanoacetate-technical in a small beaker 5 cc. of **twice** normal alcoholic potassium hydroxide. Cover the beaker with a watchglass and warm on a hot plate for five minutes. Acidify one half of the solution with dilute sulfuric acid and add a few drops of ferric ammonium sulfate T.S.: a red color develops.

Add 1 cc. of 10 per cent ferrous sulfate T.S. to the other half of the solution and warm for another five minutes. Make the solution acid to litmus paper with diluted sulfuric acid: a blue color develops in the solution.

Add 1 cc. of **twice** normal alcoholic potassium hydroxide to 5 cc. of a 10 per cent alcoholic solution of isobornyl thiocyanoacetate-technical: a yellow color forms, which rapidly changes to deep orange.

Dissolve 10 Gm. of isobornyl thiocyanoacetate-technical in 25 cc. of a saturated solution of potassium in methanol hydroxide and reflux on the steam bath for two hours. Pour the solution into 500 cc. of saturated sodium chloride solution and then acidify with hydrochloric acid. Filter the precipitate on a Buchner funnel, wash with saturated sodium chloride solution and air-dry on the filter. Dissolve the precipitate in petroleum ether, add 20 Gm. of anhydrous sodium sulfate, stopper and let stand for several hours. Filter, then evaporate the filtrate to a small volume and cool in an ice bath to effect crystallization. Filter off the crystals, wash with a few cubic centimeters of cold petroleum ether and air-dry: the isolated isoborneol melts from 200 to 205 C.

Determine the nitrogen content of isobornyl thiocyanoacetate-technical by the Kjeldahl procedure: the amount of nitrogen found is not less than 4.6 per cent, which is equivalent to an isobornyl thiocyanoacetate content of 80 per cent.

ISOBORNYL THIOCYANOACETATE LOTION

Pipet 10 cc. of bornate lotion into a graduated 100 cc. separatory funnel. Add 50 cc. of ether and shake vigorously. Add 10 cc. of ethanol and shake the contents of the flask to break the gel. Allow the funnel to stand and then draw off the lower layer. Dilute the solution in the separatory funnel to 100 cc. with ethanol. Transfer a 10 cc. aliquot to a Kjeldahl flask and determine its nitrogen content: the amount of isobornyl thiocyanoacetate-technical is not less than 90 per cent and not more than 110 per cent of the claimed amount.

WYETH INCORPORATED, PHILADELPHIA 3

Lotion Bornate: 60 cc. and 3.785 liter bottles. An emulsion containing isobornyl thiocyanoacetate 5 per cent, dioctyl sodium sulfosuccinate 0.6 per cent in mineral oil 5 per cent, gelatin 0.6 per cent and water.

JOHNSON & JOHNSON, NEW BRUNSWICK, N. J.

Hemo-Pak Absorbable Gauze Packing Strip (4 ply): 2 by 14 inches (5.08 by 35.56 cc.) and ½ inch by 2½ yards (1.27 by 228.6 cc.) in sealed tubes.

Hemo-Pak Absorbable Cotton Pad: 2 by 6 inches (5.08 by 15.24 cc.) in sealed tubes.

U. S. trademark registration pending.

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SATURDAY APRIL 24, 1948

THE JOURNAL INDEX

Because of the continued absence of the compositors from work in the printing department, the index for volume No. 136 of THE JOURNAL will be published later.

VISUAL TRAINING FOR MYOPIA

In 1920 William H. Bates published a book, "Perfect Sight Without Glasses," in which he advanced the hypothesis that visual derangements and refractive errors are due to a deformation of the eyeball resulting from a nervous and muscular strain from the superior and inferior oblique muscles and that the ciliary muscle has nothing to do with focusing the eye. He developed a corrective treatment consisting of eye exercises described as "blinking," "winking," "nose reading," "palming" and "sunning." Established clinical and scientific observations do not support the Bates thesis. Lancaster[1] felt, however, that "buried in a mass of what to the ophthalmologists seem foolish gestures and performances, there are sound and fruitful ideas." Since seeing is only half ocular, according to Lancaster's statement, the other half being cerebral, repetition, practice and exercise are capable of building up a substratum of memories useful for the interpretation of sensation and formation of syntheses which are the larger part of seeing. Duke-Elder[2] pointed out in his review of Huxley's "The Art of Seeing" that visual defects are sometimes muscular in origin, sometimes pyschologic. The competent ophthalmologist treats the former with curative exercises, while the pyschologic approach is used for the mental aspect.

From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital and University comes a report on the results obtained in the treatment of myopia by visual training. According to Alan C. Woods,[3] 103 myopic persons were subjected, after preliminary examination, by a group of optometrists and psychologists to a course of visual training designed to improve their uncorrected vision. Improvement was noted in 30 of the group (29 per cent). It was considered that the improvement was due to education in the correct interpretation of a blurred visual image. In some of the patients exercises produced a beneficial psychologic reaction toward their visual handicap, regardless of whether an actual improvement in visual acuity had occurred. With the possible exceptions of educating some patients to interpret blurred retinal images more carefully and of convincing some others that they could see better even though there was no actual improvement, this study indicates that the visual training used on these patients was of no value for the treatment of myopia.

A similar study carried out by Hildreth[4] and co-workers at the department of ophthalmology of the Washington University and the Oscar Johnson Institute brought forth the following observation and conclusions: Fifty-four selected patients with myopia were given a course of visual training which was preceded and followed by a complete ophthalmologic examination. The training was given by an optometrist while the pretraining and post-training examinations were made by a group of ophthalmologists. Thirty of the patients showed no change in their acuity, while 12 manifested a definite improvement, the best results being obtained in the subjects with low degrees of myopia. Twelve patients showed a change so slight as to be excluded in the results. The change in the improved group averaged 27 per cent. There was no change in the refractive error and no significant alteration in the ocular neuromuscular mechanism. The improvement, it was believed, probably occurred because of an improvement in reception due to stimulation of the visual effort, as the best results occurred in those patients whose pre-

1. Lancaster, W. B.: Present Status of Eye Exercises for Improvement of Visual Function, Arch. Ophth. 32:167 (Sept.) 1944.

2. Duke-Elder, S.: The Art of Seeing, by Aldous Huxley; book review, Arch. Ophth. 30:582 (Oct.) 1943.

3. Woods, A. C.: Report from the Wilmer Institute on the Results Obtained in the Treatment of Myopia by Visual Training, Am. J. Ophth. 29:28 (Jan.) 1946.

4. Hildreth, H. R., Meinberg, W. H., Milder, B., Post, L. T., and Sanders, T. E.: The Effect of Visual Training on Existing Myopia, Am. J. Ophth. 30:1563 (Dec.) 1947.

training acuity was less than would be expected from their refractive error. It was considered that visual training has a definite but limited value in some myopic patients, predominantly in those whose vision does not correspond with their known myopia.

Visual training merits further study from the ophthalmologists, particularly in relation to progress in myopia. However, the careful scientific studies that have been made now prove that the slogan "Throw away your glasses and have perfect sight" is a dangerous suggestion. The benefits from muscular training alone are a minimal aid in the proper assistance to faulty vision.

Current Comment

MEDICAL EDUCATION IN PUERTO RICO

Puerto Rico does not have a medical school. Unquestionably Puerto Rico suffers from a shortage of physicians and particularly from a shortage of competent physicians. As was pointed out by the commission headed by Dr. Ernest E. Irons which visited Puerto Rico recently, the Puerto Rican government arranged for the admission of a number of physicians who could not meet the standards of North American licensing boards or of the Council on Medical Education and Hospitals of the American Medical Association. Those who promoted this procedure argued that these physicians would locate in the rural areas and small towns and thus make available medical service to persons who could not secure it. Actually, many of these physicians drifted promptly into the larger cities and proved again that economic factors involved in determining the location of physicians for practice dominate other considerations. Now the proposal has been made by a group of Polish physicians associated during the war with the University of Edinburgh, which made available to them its laboratory facilities for the establishment of a medical school in which medicine was taught in Polish, to move the institution to Puerto Rico and organize a medical school along European lines with funds which are promised from the so-called Paderewski Foundation. Reports say that some $4,000,000 are available for the purpose. Whether such a project could succeed is extremely doubtful. Medical schools are not made in a day or a night. The quality of the faculty is dependent on its ability to secure competent teachers in the basic sciences and clinical teachers of experience in sufficient numbers to give individual instruction to prospective physicians. Since the proposed faculty did most of its teaching in Polish while resident in Edinburgh, some doubt arises as to the ability of the same faculty to teach successfully in either English or Spanish, should they become established in Puerto Pico. Certainly before any positive action is taken a most thorough investigation should be made as to the medical educational standards to be followed, since the organization of a medical school of less than a minimum standard for medical education that prevails in the United States would be a wasteful expenditure of time, energy and foundation. In the meantime through proper cooperation between leaders of medicine in Puerto Rico and those in the United States increasing efforts should be made to accommodate from thirty to fifty young properly qualified Puerto Rican students annually in the medical schools of the United States.

BIOLOGIC AVAILABILITY OF PROTEIN

A new procedure for measuring the biologic availability of proteins consists in removing surgically about 70 per cent of the liver of rats previously fed a high calory , protein-free diet and measuring the replacement of this liver protein during a recovery phase.[1] Some replacement of liver protein occurs even on a protein-free diet as the result of mobilization of tissue proteins. Feeding gelatin and zein lead to no more regeneration of protein than does the nonprotein diet. Wheat gluten gives a moderate increase, liver protein and casein a larger increase; fibrin and whole egg protein result in the greatest increase in liver protein regeneration. The results confirm those obtained by the nitrogen balance method.

TUBULAR REABSORPTION OF INORGANIC SULFATE

The ability of the kidney tubules to reabsorb normal levels of essential constituents of plasma and to allow excess amounts to pass on into the urine constitutes a principal mechanism for the control of the blood level of these substances. Waste products do not show so definite a threshold; in the case of creatinine, none is reabsorbed and all that is filtered through the glomerulus passes into the urine. A recent study[1] of the excretion of sulfate reveals that this substance has a sharp renal threshold at a level which corresponds to the normal concentration in plasma. At higher plasma levels, the tubular reabsorption remains constant and excess sulfate is excreted. The existence of this threshold would seem to suggest that the small amount of sulfate in the blood, which has heretofore been considered to be simply excretory, plays some metabolic role.

1. Vars, H. M., and Gurd, F. N.: Am. J. Physiol. 151 399, 1947

1. Lotspeich, W. T.: Am. J. Physiol. 151: 311, 1947.

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

April 22, 1948.

Debate Cause of Shortage of Physicians in Maryland

A Cumberland County general practitioner has squared off with the members of the medical profession in Maryland over the reason for the shortage of physicians. Dr. Charles S. Maxon, president of the Medical and Chirurgical Faculty of Maryland, the State Association of Physicians and Surgeons, said that it is harder to get the services of a physician because, among other things; patients abuse physicians by calling them at all hours over minor aches and pains; physicians like the forty hour week, and medical schools turn out too many specialists and not enough general practitioners. Dr. Richard J. Williams of Cumberland County took issue with views of Dr. Maxon and declared that " unless you men at the top speedily mend your ways and stop trying to shift the responsibility onto the shoulders of the few of us who are doing general medicine, then the public will rise up and give us state medicine whether we like it or not."

Chest X-Ray Drive Going Down Embassy Row

Foreign embassies are cooperating in the national chest x-ray drive now being conducted throughout the country. A survey machine paid its first visit to the Chinese Embassy in a series of stops that will include the whole diplomatic corps. A portable x-ray machine will visit the British Embassy for examination of Lord Inverchapel, retiring ambassador, and members of the staff and their families. Australia, New Zealand and the Union of South Africa are next on the list, to be followed by sixty-five other embassies, legations and missions.

Study Use of Penicillin to Prevent Infant Blindness

Dr. Joseph S. Spoto, senior surgeon in the Venereal Disease Division of the U. S. Public Health Service, said preliminary studies reveal that penicillin may be a safer and more effective substance than silver nitrate to prevent blindness among newborn infants. He disclosed in a letter to Representative Huber, Democrat of Ohio, that the use of penicillin for this purpose is now under test. He explained that penicillin can be applied either by eye droppers as with silver nitrate or by treating the mother with the drug several days before the birth of the child. Laws of most states now require that a mild solution of silver nitrate be applied to an infant's eyes as a protection against infection.

Senators Testify for Heart Institute Bill

Senators of opposite political allegiance testified in support of a bill to establish a National Heart Institute under the U. S. Public Health Service, a bill which is sponsored by Senators Bridges and Ives, Republicans, and Senators Pepper and Murray, Democrats. In addition to Bridges and Pepper, witnesses included interested members of the House of Representatives and Federal Security Administrator Oscar R. Ewing, who declared that " The extension of Federal aid for heart disease research and control is indispensible to any coordinated, large scale attack on the problem." The bill would also authorize the Surgeon General to conduct and foster research, provide grants to universities, hospitals and other agencies for heart disease study and establish research fellowships at the institute and elsewhere. Also proposed is a national Heart Council to advise the Surgeon General and authorize him to make grants in aid to states and other agencies for prevention, diagnosis and treatment of heart disease. Surgeon General Leonard E. Scheele, of the Public Health Service, and representatives of the American Heart Association also testified.

Dr. John R. Heller Heads National Cancer Institute

Dr. John R. Heller, former head of the Venereal Disease Division of the U. S. Public Health Service has been appointed director of the National Cancer Institute of Bethesda, Md. He succeeds Dr. Leonard A. Scheele, who has been appointed Surgeon General of the U. S. Public Health Service. Dr. Heller will supervise the federal cancer program, including research conducted at Bethesda laboratories, research grants to other laboratories and hospitals, and federal aid in teaching and cancer control work.

Mrs. Meyer Urges Revamping of Nation's Social Agencies

Mrs. Eugene Meyer, wife of the chairman of the board of the *Washington Post*, told a local group that there is need for cooperation of social agencies and a united effort to coordinate the nation's "cluttered community services." She criticized Dr. Alfred C. Kinsey's "Sexual Behavior of the Human Male "as a flagrant misuse of the scientific method.

Medical Legislation

Mississippi

Bill Enacted.—H. 386 was approved March 23. It provides for the appropriation of $510,000 to the state medical education board for the purpose of carrying out the provisions of the law relating to medical scholarships and loans.

New Jersey

Bill Enacted.—S. J. R. 5 has become Joint Resolution No. 2 of the Laws of 1948. It designates the month of April as Cancer Control Month throughout the state of New Jersey and urges citizens thereof to give support to the American Cancer Society and its cancer control program.

New York

Bill Enacted.—S. 2524 has become chapter 695 of the Laws of 1948. It provides for the establishment of a state university and directs such state university to formulate plans and make recommendations for the establishment of two health and medical centers as a part thereof.

South Carolina

Bill Enacted.—H. 1457 has become Governor's Act No. 798 of the Acts of 1948. It authorizes the acquisition of land for a site for a teaching hospital in the city of Charleston for use by the Medical College of South Carolina.

Virginia

Bills Enacted.—H. 439 was approved April 1, 1948. It requires every practicing medical doctor to obtain a revenue license.

S. 177 was approved April 1. To amend the hospital lien law, it increases the extent of such lien in favor of hospitals and physicians.

GOVERNMENT SERVICES

ARMY

PROGRAM FOR RESERVE OFFICERS

A committee of scientists and engineers who hold commissions in the Organized Reserve Corps met at the Pentagon Building March 26-27 to consider the Army's proposed research and development reserve program. The committee approved the contemplated program and recommended its immediate establishment; it recommended also procedures for optimum use of the technologic skills of all reserve officers engaged in the medical, biologic, physical and engineering sciences. With Brig. Gen. Norman W. Lack of Wilmington, Del., as chairman, the committee included representatives of various aspects of research, both governmental and industrial, scientific societies and educational institutions.

Under the proposed program, reserve officers who are professional scientists would be enabled to pool their knowledge for concentrated attack on Army research and development problems; it is contemplated that the program will result in effective mobilization assignments for key scientists to insure rapid mobilization in event of emergency. The first of the research and development reserve groups formed under this program was established in Wilmington, Del., in 1947 under the leadership of Brig. Gen. Lack. Similar units are being established in Philadelphia and Urbana, Ill. When the program has been approved, it is anticipated that similar groups will be instituted throughout the country.

NEW ASSIGNMENTS IN SURGEON GENERAL'S OFFICE

The Surgeon General's Office announces the following new assignments: Col. Clifford G. Blitch, chief, Medical Consultants Division; Lieut. Col. Otis W. Snyder, office of the chief, Personnel Division; Major Kenneth E. Ranson, chief of the Enlisted Branch, Personnel Division; Major Marion C. Stith, executive officer of the Hospital Division; Major William J. Clegg Jr., chief of the Administrative Branch, Hospital Division; Capt. Ula M. Morgan, assistant chief, Hospital Standards and Inspection Branch, Hospital Division, and Capt. Joseph D. Nolan, chief, Medical Regulating Branch, Hospital Division.

MEDICAL MEETING IN KOREA

About sixty officers of the medical department attended the monthly meeting at the 377th Station Hospital in Korea on March 24, at which the hospital commandant, Col. Herbert J. Witt, M.C., presided at the afternoon session. A symposium was presented on Korean medical education in which Capt. J. Richard Compton, M.C., chief of medical service at the hospital, discussed "Korean Medical Education Under New Influences"; Mildred Barody, R.N., Department of Labor, "Experiences in Organizing Industrial Medical Care"; Capt. Irwin L. Selvage Jr., M.C., "Roentgenologic Methods and Results"; Dr. Keum S. Sohn, director; Seoul Red Cross Hospital and chairman of the board of trustees, Korean Medical Association, "Current Problems in Hospital Management," and Lieut. Morton Palken, M.C., "Exigencies of a Surgical Practice Under Economic Stress." In the morning a case of kala-azar in a Korean refugee was presented, also papers on "Hospital Supply Procedures" by Capt. Louis J. Chaput, M.S.C., and "Reports of Surveys" by Capt. James O. Darling. Following a business meeting at which Col. Charles P. Ward, 24th corps surgeon, presided, a buffet supper was served at the Nan San Hotel.

ARMY INSTITUTE OF PATHOLOGY

Dr. Arthur T. Hertig, assistant professor of obstetrics, Harvard Medical School, Boston, discussed "Human Development in Its Earliest Stages" before the staff of the Institute in Washington, D.C., March 24.

Dr. Hans F. Smetana of the Institute of Pathology talked on "Periarteritis Nodosa Medionecrosis and Dissecting Aneurysms" at George Washington University School of Medicine March 19.

During April the institute held exhibits at the following places: annual meeting of Ohio State Medical Association, Cleveland; American Association for Health and Physical Education, Kansas City, Mo.; celebration of Army Week, Boston, and at the annual meeting of the National Conference of Social Workers, Atlantic City, N. J.

AIR FORCE

N.R.C. COMMITTEE VISITS RANDOLPH FIELD

The committee on Aviation Medicine of the Division of Medical Sciences, National Research Council, visited the Air University School of Aviation Medicine, Randolph Field, Texas, April 3 to review its research activities and to hold a seminar on a specific phase of aviation medicine.

Among the visitors were: Dr. Detlev W. Bronk, Johnson Research Foundation, University of Pennsylvania, (chairman); Dr. Wallace O. Fenn, University of Rochester, Rochester, New York; Dr. John C. Flannagan, University of Pittsburgh; Dr. H.K. Hartline, University of Pennyslvania, Philadelphia; Dr. George L. Maison, Boston University School of Medicine; Dr. Craig L. Taylor, University of Southern California, Los Angeles, and Dr. E. J Baldes, Mayo Clinic Aero-Medical Unit, Rochester, N. Y.

Accompanying the scientists were: Col. O.O. Benson Jr., Chief of Research, Air Surgeon's Office; Capt. Winfred P. Dana, research director, Bureau of Medicine and Surgery, Washington, D.C.; Wing Comdr. B.R. Brown, Institute of Aviation Medicine, Toronto, Canada, and Wing Comdr. J.H. Neal, Medical Air Attache, British Embassy, Washington, D.C.

SPECIAL RESEARCH POSITION OPEN

The Air University School of Aviation Medicine, Randolph Field, Texas, is in receipt of an announcement from Headquarters, U.S. Air Force, that the school has been allotted one of a limited number of special research positions authorized by Congress to attract outstanding scientists to service laboratories. The School of Aviation Medicine intends to utilize the new allocation, which carries with it a salary of $10,000 to $15,000 per annum, to establish a civilian position for a director of research. Inquiries concerning this vacancy should be addressed to the commandant.

NAVY

MEDICAL OFFICERS CERTIFIED BY BOARDS

The Bureau of Medicine and Surgery announces that as of March 30, one hundred and thirty-nine medical officers of the Regular Navy have been certified by American specialty boards, and that two hundred and five medical officers had completed graduate training courses of six months to one year's duration in various specialties during 1947. Of this number, eighty-seven were trained in civilian institutions and one hundred and eighteen in naval hospitals. Additional medical officers will be eligible for examinations by specialty boards within the next few months.

PLAN ADDITIONAL RESERVE MEDICAL DIVISIONS

A new organization plan for inactive volunteer reserve units of the Navy Medical Corps, which provides for the formation of two hundred and forty reserve medical divisions throughout continental United States, has been placed in effect. To date one hundred and forty-four reserve medical divisions have been organized in the eleven continental Naval Districts and the Potomac River Naval Command. Members of the inactive volunteer reserve are assigned to the individual medical division in accordance with their professional qualifications. Their assignment, however, carries no additional obligations or responsibilities other than those which the members are willing to assume. The new plan permits the administration of a training program for inactive reservists, including medical division meetings at which qualified instructors present subjects peculiar to military medicine; in addition, special training courses on some of the subjects may be arranged.

THE SURGEON GENERAL'S SYMPOSIUM

The symposium of the Surgeon General with all district medical officers, medical officers in command of naval hospitals and other medical activities will be held at Bethesda, Md., May 27-29. The subjects discussed will include the organization of the Bureau of Medicine and Surgery, the graduate training program, formation of reserve divisions, modernization of equipment in naval hospitals, medical aspects of atomic energy, procurement and personnel, planning and logistics. In addition to naval officers, the speakers will include the Honorable John L. Sullivan, Secretary of the Navy, and Dr. Henry L. Bockus of Philadelphia.

NEW REGULAR OFFICERS

The following physicians have been commissioned in the Medical Corps of the Regular Navy: Comdr. LeRoy E. Wible, Albuquerque, N.Mex., and Lieut. John T. Egan Jr., Jamaica, N.Y.

The following graduates of the Navy's V-12 program have accepted commissions in the Regular Navy Medical Corps: Lieuts.(jg) John P. Ahearn, Somerville, Mass.; Carleton J. Brown, New London, Conn.; Robert J. Evoy, Seattle; Arthur A. Helgerson, Attleboro, Mass.; James H. Lee Jr., Wilmington, Del.; Joseph E. F. Rankin, Baltimore; Myron E. Samuelson, Genoa, Neb., and Julius H. Spence, Austin, Texas.

VETERANS ADMINISTRATION

MEDICAL ADMINISTRATIVE OFFICERS WANTED

The U. S. Civil Service Commission is accepting applications to fill high level administrative positions with the Veterans Administration in the field of medical administration. These positions are open in the central office of the Veterans Administration in Washington, D. C., and in branch offices and hospitals throughout the country. The salaries range from $7,102 to $9,975 a year. In the central office the duties of these positions are in part as follows: developing policy, determining methods and supervising such administrative activities of veterans' hospitals and national homes as admissions, discharges, transfers and food requirements. In the branch offices the duties are to supervise the program for medical administration and to coordinate it in centers, hospitals, homes and regional offices of the branch area. In the veterans' hospitals the duties of these positions are to coordinate and direct the activities of hospitals within the scope prescribed by the deputy administrator or the Department of Medicine and Surgery, by formulating and executing local policies and by carrying out plans issued by higher authorities; also, to administer the medical activities of the hospital through the chief medical officer.

Applicants must be citizens of or owe allegiance to the United States, or be citizens of the Republic of the Philippines. Applications should be made on circular EC-11, which shows the administrative experience requirements for these positions. Persons interested should apply not later than April 14, 1948 to the U. S. Civil Service Commission, Washington, D. C.

HOSPITAL CONSTRUCTION AT NEW HIGH

Lieut. Gen. Raymond A. Wheeler, chief of Army engineers, announces that twenty-three veterans' hospitals are now under construction and when completed will provide an additional 10,306 beds. During the first quarter of 1948 contracts were let for twelve general hospitals and bids on two additional hospitals were advertised. In addition, forty-six hospitals are still in the process of design; forty others have progressed sufficiently to be scheduled for advertising. During the present year the five hospitals which have not yet been scheduled for advertising include the six hundred bed tumor clinic in Chicago and four general hospitals to be constructed in Boston, New York, Syracuse and Washington, D.C. Of seventy-one hospitals scheduled for construction by the Corps of Engineers under the Veterans Administration program, five had been designed by the Agency prior to the engineers' participation in the program. General Wheeler also announced that contracts had been awarded for the nine hundred and ninety-nine bed hospital in Albany, N.Y. The total amount of the six contracts involved is $14,445,727. Construction progress on the Veterans Administration hospital program has doubled that of last year, General Wheeler said. The increased construction costs necessitated the redesigning of practically all hospitals that had not been actually placed under contract.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

CALIFORNIA

Medical Garden Club Show.—The Los Angeles County Medical Garden Club will present the regular Spring Flower Show in the lounge of the Los Angeles County Medical Association headquarters building on April 29-30. This show will be opened to the public without admission charge April 19 from 12 noon to 9 p.m. and Friday, April 30, from 9 a.m. to 9 p.m. Entries will be accepted from doctors of medicine. Flower arrangements only may be entered by the wives of physicians and members of the physicians office personnel.

COLORADO

Laboratories Approved for Blood Tests.—The state department of public health has approved twenty-two laboratories in Colorado to perform premarital and prenatal blood tests. Their certificates of approval will expire Dec. 31, 1948 but may be renewed. These laboratories were required to pass inspection. Each received two hundred blood specimens and was required to obtain an average of not less than 99 per cent correct results on the nonsyphilitic specimens and not less than 90 per cent on the syphilitic specimens as compared with the results of the control laboratories. Clerks in marriage license bureaus have been instructed to accept blood tests only from approved laboratories, a list of which may be secured by writing Marjorie Van Vranken, Secretary, Evaluation Committee, 430 State Office Building, Denver.

State Health Department Reorganizes.—In the recent reorganization of the Colorado State Department of Public Health all sections dealing with medical care and services have been put under a director of Preventive Medicine Services. Those sections whose activities are used by all other units in the department, such as administration, health education, records and laboratories, have been placed in the Division of General Services, thus eliminating the need for their duplication in various sections. All sanitation activities will be under the direction of the Division of Sanitary Services. Three new services under full time directors have been added: health education, hospital facilities and veterinary medicine. Increased budget and personnel have made it possible to provide more service to local areas in the form of consultation and advisory visits on both old and new programs and to begin services which previously had not been available.

CONNECTICUT

Memorial to D. Chester Brown.—A gift of several thousand dollars has been contributed to the building fund of the Connecticut State Medical Society by the friends and patients of the late Dr. D. Chester Brown. Dr. Brown was a trustee of the American Medical Association from 1918 to 1930. He was president of the Connecticut State Medical Society in 1913 and president of the Fairfield County Medical Association in 1908.

New Medical Building in Hartford.—Construction of an eight story medical building to provide suites of offices for about ninety physicians was recently begun in Hartford. The building is being erected by the Connecticut Mutual Life Insurance Company adjacent to the new addition to the Hartford Hospital.

ILLINOIS

Nursing Homes.—The state department of public health has licensed two hundred and twenty-two nursing homes and exercises supervision over them. Peoria County heads the list with 565 beds. Cook County, outside Chicago, has twenty-one nursing homes with a bed capacity of 1,144. A directory of all nursing homes in Illinois that are licensed by the Illinois State Department of Public Health is available on request to the department's Division of Sanitary Engineering, Springfield.

Chicago

Goodspeed Memorial Fund.—The Charles B. Goodspeed Memorial Fund has been started in memory of the late former president and benefactor of Presbyterian Hospital. Other friends of Mr. Goodspeed are being invited to join with staff contributors in providing the fund. Drs. William G. Hibbs and Harry Boysen comprise the medical staff committee in charge of the project. Checks made payable to Presbyterian Hospital and designated for the Goodspeed Memorial Fund may be sent to the committee. Pledges payable over a period of five years also are sought.

INDIANA

New Section Created.—A section on obstetrics and gynecology of the Indiana State Medical Association has been organized with Dr. Dudley A. Pfaff, Indianapolis, chairman, and Dr. Edgar L. Engel, Evansville, secretary.

Medical Alumni Day.—The first Alumni Day of the Indiana University School of Medicine will be held on the Medical Center campus in Indianapolis on May 5, also Founders Day of the university. A clinical program will be held in the auditorium of the medical school from 9:30 to noon. Luncheon at 1p.m.will be followed by a general session at 2 p.m.

IOWA

State Journal Dedicated to Dr. MacEwen.—The April issue of the *Journal of the Iowa State Medical Society* has been designated the Dean MacEwen Memorial Issue and contains articles contributed by the staff of the State University of Iowa College of Medicine, where Dr. Ewen M. MacEwen served as dean from 1935 to 1947. Problems of medical education, research and hospitals are discussed in the issue.

MAINE

Dr. Crosby Honored.—More than three hundred and fifty townspeople of Milo honored Dr. Nathaniel Crosby at a town hall meeting February 23, on the occasion of his eighty-fourth birthday and his fifty-seventh year of service as a physician. The Rotary Club of Bangor shared in the proceedings, and the Maine Medical Association sent greetings. Many tributes were paid to Doctor Crosby for his years as a general practitioner.

MASSACHUSETTS

Harvard Increases Tuition.—An increase in tuition for all students at Harvard Medical School and Harvard University Dental School, Boston, was announced April 5. Tuition in both schools, which has been $580 a year since 1945, will be raised to $800 a year beginning in the fall term of 1948. Officers of the two schools assured students that loan funds and scholarships are at hand to assist individuals in meeting the increased cost. Additional scholarship funds will be available next autumn.

MINNESOTA

Personal.—Charles Sheard, Ph.D., Director, Division of Physics and Biophysical Research, Mayo Clinic, Rochester, Minn., was guest of honor at a dinner in Washington, D.C., March 11, at which Surgeon General Clifford A. Swanson, U.S. Navy, and representatives Dewey Short of Missouri and Arthur L. Miller of Nebraska were among the speakers.

Public Health Nursing Services.--Since the passage a year ago of the state law subsidizing public health nursing, eleven counties of Minnesota have established public health nursing services and eight have taken advantage of the subsidy provisions to employ additional nurses. The state now has four hundred and sixty-four public health nurses, about equally divided between large cities and rural areas.

NEBRASKA

Dedicate Childrens Memorial Hospital.—The dedication in Omaha of the Childrens Memorial Hospital was held in February. According to newspaper reports more than 30,000 persons from Nebraska and surrounding states contributed to the hospital fund. The hospital adds more than one hundred beds for the treatment of children and will make available improved facilities for study and research in growth and development. The combined staffs of Creighton University School of Medicine and University of Nebraska College of Medicine make up the medical organization of the hospital.

NEW JERSEY

Annual State Medical Meeting.—The Medical Society of New Jersey will hold its annual meeting at Haddon Hall, Atlantic City, April 26-29. The program is made up largely of section meetings in which members of the society and guest speakers will take part. At the general session Wednesday afternoon, Mr. Arthur L. Conrad, Chicago, will speak on "Implications of Socialized Medicine" and Dr. Isidore Snapper, New York, on "Medicine Is Global." The dinner dance will be Wednesday at 7:30 p.m. The guest speaker will be John C. Krantz Jr., Ph.D., Baltimore, "The Simplicity to Wonder." Scientific, educational and technical exhibits have been arranged. The Woman's Auxiliary will meet in conjunction with the state society.

NEW YORK

Postgraduate Lectures.—The following postgraduate lectures have been arranged by the Medical Society of the State of New York in cooperation with the New York State Department of Health:

Sullivan County Medical Society

April 21 George P. Heckel, Rochester, Practical Application of Endocrines in Gynecology, Workmen's Circle Sanatorium, Liberty, 8:30 p.m.
April 28 Clyde L. Randall, Buffalo, Office Management of Female Pelvic Disorders, Lenape Hotel, Liberty, 8:30 p.m.
May 5 Ferdinand J. Schoeneck, Syracuse, Sterility, Monticello Hospital, Monticello, 8:30 p.m.
May 12 Chester E. Clark, Syracuse, Gynecology in General Practice, home of Dr. Harry Golembe, Liberty, 8:30 p.m.

Nassau County Medical Society

April 27 A. W. Martin Marino, Brooklyn, Early Diagnosis of Cancer of Rectum, Garden City Hotel, Garden City, Long Island, 9:00 p.m.
May 25 Robert M. Marcussen, New York, Treatment of Migraine, Cathedral House, Garden City, Long Island, 9:00 p.m.

The Ontario County Medical Society will hear Dr. Jacob D. Goldstein, Rochester, speak on diseases of the liver, at Canandaigua Hotel, Canandaigua, April 13, 8 p.m. On May 13 Dr. Richard S. Farr, Syracuse, will address the Jefferson County Medical Society at Hotel Woodruff, Watertown, 8:30 p.m., on treatment of low back pain.

PENNSYLVANIA

County Society to Honor Dr. Bortz.—A homecoming celebration in honor of Dr. Edward L. Bortz, Philadelphia, President of the American Medical Association and a native of Westmoreland County, is being sponsored by the Westmoreland County Medical Society on May 5-6. A public health meeting in the Greensburg High School Auditorium on May 5, 8:15 p.m., with Dr. Bortz speaking on "Health as Our Fundamental National Resource" will start the celebration. Others to speak at this public meeting will be: Dr. Norris W. Vaux, Philadelphia, secretary of health; Mr. Lester H. Perry, executive secretary of the state society; Dr. Chauncey L. Palmer, Pittsburgh, chairman of the Committee on Public Health Legislation; Dr. Oliver E. Turner, Pittsburgh, member of the commission on Public Health and Preventive Medicine; and Dr. Pascal F. Lucchesi, superintendent and medical director of Philadelphia General Hospital, Philadelphia. On Thursday, beginning at 10 a.m., an all scientific program will be held at the Westmoreland County Hospital Dr. Elmer Hess, Erie, president of the Medical Society of the State of Pennsylvania, will discuss "Urologic Hints for the General Practitioner." Six other specialists will appear on the morning program. Speakers at the session to be held at the Greensburg Country Club will be:

Dr. James E. Paullin, Atlanta, Ga., Peptic Ulcer, Pathogenesis and Medical Approach.
Dr. Waltman Walters, Rochester, Minn., Surgery in Peptic Ulcer.

Dr. Paullin will also talk on the "Management of Severe Diabetes" and Dr. Walters on "Advance in Treatment of Lesions of the Biliary Tract."

WISCONSIN

International College of Surgeons.—The Wisconsin Chapter of the International College of Surgeons will meet April 28 for a dinner at 6:15 p.m. and a scientific program at 8 p.m. at the University Club of Milwaukee. Papers to be presented are on the following topics: surgery of the rectosigmoid; diagnostic and therapeutic management of difficult surgical case; repair of large postoperative ventral hernia; fenestration operation for the improvement of hearing; high tension line injury--electric burns, and Wilm's tumor--case report.

GENERAL

Congress of German Internists.—Members of the American Medical Association are invited to attend the Congress of German Internists May 19-21 in Karlsruhe. An attendence of two thousand specialists in internal medicine is expected. Subjects to be discussed at the Congress are "The Vegetative Nervous System," "The Coloring Matter of the Blood" and "Virus Diseases."

Association for Study of Goiter.--The American Association for the Study of Goiter will meet at the King Edward Hotel, Toronto, Canada, May 6-8, under the presidency of Dr. James H. Means, Boston. Among the subjects of the guest speakers, will be the relationship of hyperthyroidism to myasthenia gravis; the hazards and limitations of radioactive isotopes; treatment of hyperthyroidism with radioactive iodine; effect of total thyroidectomy on the function of metastatic cancer of the thyroid, and the surgical treatment of the thyroid disease.

Psychiatrists Appoint Medical Director.—Dr. Daniel Blain, formerly chief of neuropsychiatric services for the Veterans Administration, has accepted the newly established position of medical director of the American Psychiatric Association. Dr. Blain will continue to reside in Washington, D. C. For the present he may be addressed at Georgetown University Hospital, Washington, D. C., or at the executive office of the association, Room 924, 9 Rockefeller Plaza, New York 20. Mr. Austin M. Davies, who has been with the association for fifteen years, will continue as executive secretary, with headquarters in the New York office.

Lippincott Library Award.--The American Library Association Committee on Awards announced that the Joseph W. Lippincott Award for Distinguished library service during 1947-1948 will be given at the association's conference in Atlantic City, N. J., June 13-19. It consists of a $500 gift and a certificate presented by the donor. Names of nominees should be submitted to John M. Cory, chairman, Americal Library Association Committee on Awards, University of California, Berkley, Calif., Mary N. Barton, Enoch Pratt Free Library, Baltimore, Md., or to Ola M. Wyeth, Savannah Public Library, Savannah, by May 15. The award was temporarily discontinued in 1941.

Symposium in Ophthalmology.—A refresher symposium in ophthalmology will be given by Mount Sinai Hospital in affiliation with Columbia University College of Physicians and Surgeons, April 26 - May 22. This will consist of clinical, laboratory and didactic instruction in pathology, embryology, bacteriology, optics, surgery, ophthalmoscopy and other subjects. The class will be limited to eight qualified ophthalmologists. Information may be obtained from the Registrar of Medical Instruction, Mount Sinai Hospital, New York, or from Dr. John B. Truslow, Assistant Deam, Columbia University College of Physicians and Surgeons, New York.

World Health Assembly.--The World Health Assembly, representative of all members of the World Health Organization, will be convened in Geneva, Switzerland, on June 24, under a recent decision made by the Interim Commission, officials of the State Department announce. At present, twenty-two members and eight nonmembers of the United Nations are parties to the constitution of the World Health Organization. As the constitution does not legally come into force until twenty-six members of the United Nations become parties to it, it is hoped that additional nations, including the United States, will join the organization prior to the assembly in June. If the assembly follows the recommendations made by the Interim Commission, the World Health Organization will focus its activities during the early years on malaria, tuberculosis, venereal diseases, and maternal and child health.

Meeting of Tropical Medicine and Malaria.--The fourth International Congresses on Tropical Medicine and Malaria will be held in Washington, D.C., May 10-18 under the sponsorship of the Department of State. The last meeting of the congresses was in Amsterdam, Netherlands, in 1938. About twenty-five nations will send official delegations. Although no formal invitations have been sent to many of the medical, technical and scientific institutions, societies and organizations throughout the world, the Department of State welcomes all interested professional men and women, including students, to participate. Those who desire to attend should communicate with the Division of International Conferences, Department of State, as soon as possible. To facilitate the program, the meetings will be held in twelve sections as follows: Research and Teaching Institutes, Tropical Climate and Physiology, Bacterial and Spirochetal Diseases, Virus and Rickettsial Diseases, Malaria, Helminthic Diseases, Protozoan Diseases, Nutritional Diseases of the Tropics, Tropical Dermatology and Mycology, Tropical Veterinary Medicine, Public Health, and Medical and Veterinary Entomology. Two evening meetings will commemorate historic discoveries in tropical medicine. The first will celebrate the demonstration by Walter Reed of the mosquito transmission of yellow fever and his admission to the Hall of Fame. The second will commemorate the fiftieth anniversary of the discovery by Ronald Ross of the method of malaria transmission.

National Health Assembly--Oscar R. Ewing, Federal Security Administrator, had a meeting on March 16 of persons he selected to compose an executive committee for the National Health Assembly to be held May 1-4 in Washington, D. C. This committee suggested the number of sections which should compose the assembly and their titles, and agreed on some of the chairmen. The assembly will divide itself into the following fourteen sections: (1) Nation's Need for Medical and Health Personnel; (2) Nation's Need for Hospital Facilities, Health Centers and Diagnostic Clinics; (3) Local Health Units for the Nation; (4) Chronic Disease and the Aging Process; (5) Maternal and Child Health; (6) Rural Health; (7) Research in the Service of Health; (8) Medical Care; (9) State and Community Planning for Health; (10) Physical Medicine and Rehabilitation; (11) Dental Health; (12) Mental Health; (13) Environmental Sanitation, and (14) Nutrition in World Health. The executive committee also approved of a tentative statement of the scope of the sections. A chairman and a steering committee will be appointed for each section.

Mr. Ewing has since announced the formation of a research section of the forthcoming assembly. Dr. Andrew C. Ivy, vice president of the University of Illinois, will be chairman of the research section. While the broad area of the medical research problem will be outlined by Dr. Ivy and the committee preparatory to the convening of the assembly, the specific agenda of the section will not be formulated until its first session.

Dr. Hugh R. Leavell, professor of public health practice, Harvard University School of Public Health, will be chairman of the medical care section of the assembly. In announcing the formation of the section, Mr. Ewing stressed the importance of a thorough analysis of the problem of medical care in terms of need and existing services as they affect the patient, the physician, the hospital administrator and the public health official. Voluntary plans for financing medical care, he said, should be examined for their adequacy in terms of efficiency, quality and coverage of services, and costs within ability to pay

The environmental sanitation section of the assembly will have as chairman Arthur D. Weston, director of sanitary engineering, Massachusetts State Department of Public Health. This section will include leaders in public health and sanitary engineering; scientists in chemistry, biology and allied fields; representatives of milk and food producers, of industry and labor, and farm groups

CORRECTION

Hormonal Test for Fetal Death.--In THE JOURNAL, April 10, in the article by Zondek, Sulman and Black entitled "Hormonal Test for Fetal Death in Disturbed Pregnancy" in the eleventh line, page 968, the words 9 per cent should be 90 per cent.

Deaths

Ernest Leori Hunt ⊕ Worcester, Mass.; born in Abington, Mass., Nov. 11, 1877; Harvard Medical School, Boston, 1902; member of the House of Delegates of the American Medical Association in 1943; member of the founders group of the American Board of Surgery; past president and secretary of the Worcester District Medical Society; member and formerly vice president of the New England Surgical Society; member of the American Urological Association; past president of the Massachusetts Medico-Legal Society and the New England Cancer Society; a director of the Massachusetts Division of the American Cancer Society, serving on the professional committee since its inception in 1945; fellow of the American College of Surgeons; during World War I medical examiner for a local draft board and later a captain in the medical corps of the U. S. Army; lieutenant colonel, medical reserve corps, not on active duty; formerly associate medical examiner for the Eleventh Worcester District; pathologist at United States Veterans Hospital 89 in Rutland, Vt., from 1922 to 1931; chief of staff of the Worcester Cancer Clinic from 1929 to 1946; served on the staffs of the Day Kimball Hospital in Putnam, Conn., Harrington Memorial Hospital, Southbridge, Holden District Hospital in Holden, Grafton State Hospital, North Grafton, Worcester County Sanatorium, Worcester State Hospital and the Worcester City Hospital; surgeon in chief at the Fairlawn Hospital; a director of the laboratories of the city health department; member of the governing board of the educational division of the Y.M.C.A., member of the Worcester Historical Society and for many years a member of the board of directors of the Worcester Free Public Library; prominent in Red Cross work and in the cause of cancer control; died in the City Hospital January 17, aged 70, of coronary thrombosis.

Philip Hillkowitz ⊕ Denver; born in Russia Aug. 30, 1873; Medical College of Ohio, Cincinnati, 1879; formerly on the faculties of Gross Medical College and Denver and Gross College of Medicine; served as associate professor of chemistry at the University of Denver; specialist certified by the American Board of Pathology; founder and first president of the American Society of Clinical Pathologists; for many years chairman of the Registry of Medical Technologists; served during World War I; for many years president of the Jewish Consumptives' Relief Society; served as pathologist at the Sanatorium of the Jewish Consumptives' Relief Society in Spivak; affiliated with Beth Israel Hospital, St. Anthony Hospital and Mercy Hospital, where he died January 30, aged 74, of cerebral hemorrhage.

James Alexander Craig, Keosauqua, Iowa; Jefferson Medical College of Philadelphia, 1895; member of the American Medical Association; died January 11, aged 76.

Clifford W. Conkling ⊕ Windfall, Ind.; Pulte Medical College, Homeopathic, Cincinnati, 1900; died in St. John's Hospital, Anderson, January 13, aged 78, of cerebral hemorrhage.

Ralph David Engle, Petoskey, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1906; served as city health officer and county coroner; affiliated with the Lockwood General Hospital, where he died January 14, aged 68, of heart disease.

William H. Hardesty, Waverly, Ky.; Kentucky School of Medicine, Louisville, 1892; member of the American Medical Association; died in Evansville, Ind., January 11, aged 79, of cerebral hemorrhage.

John Albert Hayward ⊕ Providence, R. I.; Boston University School of Medicine, 1906; specialist certified by the American Board of Anesthesiology, Inc.; member of the American Society of Anesthetists, Inc.; served overseas during World War I; affiliated with the Roger Williams General Hospital, where he died January 11, aged 69.

Isaac Burton Hunt, Big Clifty, Ky.; George Washington University School of Medicine, Washington, D. C., 1912; died January 13, aged 68.

John Edward Hutchinson Jr., Birmingham, Ala.; Meharry Medical College, Nashville, Tenn., 1930; died Dec. 7, 1947, aged 43, of cerebral hemorrhage.

Marvin Israel ⊕ Buffalo; University of Buffalo School of Medicine, 1914; specialist certified by the American Board of Pediatrics; associate in pediatrics at his alma mater; assistant director of infant welfare, city health department; affiliated with the Children's Hospital and the Salvation Army Home and Hospital; died in the Buffalo General Hospital January 8, aged 56, of coronary thrombosis.

Lewis L. Jackson, Vienna, Ill.; Loyola University School of Medicine, Chicago, 1916; served as county coroner; affiliated with the Metropolis Memorial Hospital in Metropolis, where he died January 12, aged 64, of pulmonary embolism following an automobile accident on Christmas eve.

Mary Louise Jennings, Geneva, N. Y.; University of Buffalo School of Medicine, 1899; died in the Geneva (N. Y.) General Hospital January 17, aged 79.

Paul Harold Kelly, St. Paul; University of Minnesota College of Medicine and Surgery, Minneapolis 1911; fellow of the American College of Surgeons; member of the American Medical Association; for many years affiliated with St. Joseph's Hospital, where he died January 9, aged 63.

Joseph Carroll Monmonier ⊕ Catonsville, Md.; University of Maryland School of Medicine, Baltimore, 1897; served during World War I; colonel, medical reserve corps, U. S. Army, not on active duty; died recently, aged 75.

John Alva Norris, Cross Plains, Texas; Missouri Medical College, St. Louis, 1888; died in the Overall Hospital, Coleman, Dec. 2, 1947, aged 89, of arteriosclerosis.

John Alexander Porter, Philadelphia; Starling Medical College, Columbus, 1898; died recently, aged 77, of myocardial failure and arteriosclerotic heart disease.

Charles Frederic Roche ⊕ Miami, Fla.; University of Michigan Medical School, Ann Arbor, 1919; fellow of the American College of Physicians; specialist certified by the American Board of Internal Medicine; past president of the Dade County Medical Society; affiliated with St. Francis Hospital; died suddenly January 18, in Fort Lauderdale, aged 59.

Edward Holton Rogers, New York; College of Physicians and Surgeons, medical department of Columbia College, New York, 1892; member of the American Medical Association; for many years affiliated with the Knickerbocker Hospital; died in the Westchester Division of the New York Hospital, White Plains, January 5, aged 81, of arteriosclerosis.

Samual Smith, Pelham Manor, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1889; died in the New Rochelle (N. Y.) Hospital recently, aged 87.

Laurel Erceldene Samson ⊕ Franklin, Vt.; University of Vermont College of Medicine, Burlington, 1928; diplomate of the National Board of Medical Examiners; affiliated with St. Albans Hospital in St. Albans; served as health officer and member of the school board; died in the Bishop De Goesbriand Hospital in Burlington January 27, aged 45, of leukemia.

Edwin Jacob Schisler ⊕ St. Louis; Beaumont Hospital Medical College, St. Louis, 1896; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; affiliated with St. Anthony's Hospital, St. Louis City Hospital and Evangelical Deaconess Hospital, where he died January 12, aged 73.

Mae Catherine Schroder, New York; Tufts College Medical School, Boston, 1900; for many years member of the city department of health; died in the Bellevue Hospital Dec. 9, 1947, aged 75.

Adolph Shoenfield, Detroit; Harvard Medical School, Boston, 1918; member of the American Medical Association; served on the staffs of various Veterans Administration hospitals; died recently aged 57.

Abraham Joshua Siever ⊕ El Monte, Calif.; Washington University School of Medicine, St. Louis, 1934; died in Duarte Dec. 5, 1947, aged 45, of tuberculous peritonitis.

David Lewis Simon ⊕ Butler, Pa.; University of Pittsburgh School of Medicine, 1911; specialist certified by the American Board of Urology, Inc.; member of the American Urological Association; formerly practiced in Pittsburgh, where he was city fire and police surgeon and on the staff of the Montefiore Hospital; affiliated with the Butler County Memorial and Veterans Administration hospitals; died January 15, aged 58, of coronary thrombosis.

Leander Franklin Sory, Adams, Tenn.; University of Nashville Medical Department, 1898; died Dec. 13, 1947, aged 73, of hemorrhage of the lungs.

David S. Sparks, Los Angeles; American Medical College, St. Louis, 1890; died recently, aged 84.

Frank J. Stein, New York; Kentucky University Medical Department, Louisville, 1901; for many years medical director of the Denver Chemical Company; died January 10, aged 69, of cerebral hemorrhage.

John Stevens, Gonvick, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1897; member of the American Medical Association; served during World War I; for many years village health officer and head of the board of education; died Dec. 1, 1947, aged 72, of uremia.

Hamilton Stillson, Seattle; University of Louisville (Ky.) Medical Department, 1882; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; died in Seattle General Hospital January 11, aged 90, of arteriosclerosis and coronary occlusion.

Clayon Evan Stout, Raceland, Ky.; University of Louisville (Ky.) Medical Department, 1906; died January 4, aged 74, of carcinoma of the kidney.

Edgar Eugene Strickland, Citra, Fla.; Atlanta College of Physicians and Surgeons, 1904; died Dec. 8, 1947, aged 65.

Alfred Morley Switzer, Port Huron, Mich.; Detroit College of Medicine, 1897; died in Mount Clemens recently, aged 77, of arteriosclerotic gangrene of the foot.

William S. Taylor, Isola, Miss.; Memphis (Tenn.) Hospital Medical College, 1912; died Dec. 29, 1947, aged 71.

Mabel Madsen Teague, Indianapolis; Eclectic College of Physicians and Surgeons, Indianapolis, 1893; died January 9, aged 78.

Joseph Atkinson Thomas, Valdosta, Ga.; University College of Medicine, Richmond, 1908; member of the American Medical Association, died in the Little Griffin Hospital Dec. 21, 1947, aged 63, of chronic myocarditis.

Edgar Vance Thompson, Stoneboro, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1905; served during World War I; died recently, aged 69, of multiple sclerosis.

William H. Thompson, East Cleveland, Ohio; Homeopathic Hospital College, Cleveland, 1880; died January 16, aged 97, of pneumonia.

Victor Corse Thorne, Greenwich, Conn.; Cornell University Medical College, New York, 1902; died January 18, aged 76.

Donald Bertrand Tresidder, Stanford University, Calif.; Stanford University School of Medicine, Stanford University, 1927; since Sept. 1, 1943 president of Stanford University; elected to the board of trustees in December, 1939 and became president of the board in May, 1942, resigning to accept the university presidency; for many years president of the Yosemite Park and Curry Company; found dead January 28, aged 53.

William Ray Tubbs ⊕ Carbondale, Colo.; Hahnemann Medical College and Hospital of Philadelphia, 1899; affiliated with the Community Hospital in Glenwood Springs; died in Glenwood Springs recently, aged 73, of a rupture of an abdominal aorta aneurysm.

Perry Irwin Tussing, Lima, Ohio; Rush Medical College, Chicago, 1906; member of the National Gastroenterological Association; served as treasurer and president of the Allen County Academy of Medicine; affiliated with the Lima Memorial and St. Rita's hospitals; died recently, aged 80, of angina pectoris and hypertension.

David Estell Upton, Munfordville, Ky.; University of Louisville School of Medicine, 1928; member of the American Medical Association; affiliated with the Samson Community Hospital in Glasgow; died January 12, aged 45.

John Poler Walsh, Mitchell, Ore.; Harvey Medical College, Chicago, 1902; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; died in a hospital at Hermiston Dec. 12, 1947, aged 84.

S. A. Ware, Springfield, Ill.; Meharry Medical College, Nashville, Tenn., 1899; died in St. John's Hospital January 8, aged 74.

Charles Seymour Wasweyler, Milwaukee; Milwaukee Medical College, 1896; died in St. Joseph's Hospital recently, aged 78, of diabetes mellitus.

Alan Robert Will, Calhoun, Ky.; University of Louisville (Ky.) School of Medicine, 1935; member of the American Medical Association; affiliated with the Owensboro-Daviess County Hospital in Owensboro; died January 2, aged 36.

Wilburn Cook Williams, San Marcos, Texas; University of Tennessee Medical Department, Nashville, 1905; past president of the Hays-Blanco Counties Medical Society and vice president of the State Medical Association of Texas; died recently, aged 73, of coronary occlusion.

Foreign Letters

ITALY

(From Our Regular Correspondent)

Feb. 1, 1948.

Meeting of Tuberculosis Association

The Sicilian Tuberculosis Association met in Catania to discuss reports presented by members. Professor Condorelli presented a synthesis of twenty years observation on Tuberculous peritonitis, Circumscribed discrete forms of tuberculous peritonitis were defined as mute. This referred only to syndromes caused by tuberculous and protopathic peritonitis, with mild dissemination, few general manifestations, chronic course and vague abdominal symptoms. Classic pathology was considered of little aid in study of this syndrome. Observations were made and laparotomy performed because of diagnostic errors in cases in which the clinical picture had not been outlined. The symptoms consist in mild rise of temperature, general malaise, variable anemia, and frequent disturbances of organic sensibility and the vegetative nervous system. Abdominal symptomatology is indefinite and consists of functional gastric disturbances and abdominal syndromes. Pronounced sensitivity to pressure along the abdominal aorta, revealing irritation of the lumboaortic plexus, is always present.

Professor Meldolesi discussed pulmonary infiltrations whose tuberculous causation could not be demonstrated. He outlined the occurrence of a group of pulmonary lesions which the phthisiologist should know in order to avoid dangerous errors in diagnosis and treatment. So-called fugacious infiltrations must be differentiated from phthisiogenetic infiltrations, three types of which were considered by the speaker. He also discussed permanent infiltration of the type of Besnier-Boeck-Schaumann's disease with epithelioid cells and giant cells. The etiologic basis for this form is completely obscure; some authors suggest a concept of attenuated tuberculosis and others a leprous origin.

Professor Fici discussed pulmonary tonus and pulmonary neurodystonia as related to an extensive or circumscribed excitability of the vegetative nervous system. Sometimes neurodystonia may be segmental, involving a minimal area. He analyzed the pathogenesis of the different localization of the bronchial murmur in exudative pleurisy, of atelectasis (massive, acute transitory lobar, partial), and of the variations of the volume of the lungs. Of the vascular neurodystonias, Professor Fici referred particularly to hemoptysis. Vasomotor disturbances of the vegetative innervation may be influenced by the action of hormones, meteorologic variations or a concomitant hysteric syndrome. In fulminant hemoptysis the possibility of efficient action of histamine was considered. Mixed myogenetic and vascular neurodystonia may be indistinguishable. Pathogenic mechanisms of some fugacious pulmonary infiltrations may be tied to the changes of the neurovegetative tonus.

Professor Sagona reported on the national, regional, provincial and communal organization campaign against tuberculosis in Italy. Professor Paola discussed the modern points of view concerning surgical collapse therapy insisting that the favorable result of surgical treatment depends directly on the clinical and immunobiologic condition of the patient who is to be operated on and that pulmonary elasticity should be the essential criterion in selection of the type of treatment. Early forms were considered most benefited by immobilization of the lung.

Benign spontaneous pneumothorax as secondary or symptomatic and primary idiopathic groups were discussed by Dr. Fichera.

BERLIN

(From Our Regular Correspondent)

Feb. 24, 1948.

Organization of Scientific Medical Societies

The organization of German scientific medical societies in the Soviet zone has been approved by Order 124 of May 21, 1947, by Marshall Sokolowski. Such societies of specialists (surgeons, gynecologists, internists, etc.) may be organized under the direction of the minister-presidents of the *laender* and provinces in the university cities of Jena, Leipzig, Rostock, Halle and Greifswald and in cities which, including the suburbs, have more than twenty-five specialists in the particular field. The activities of these societies are controlled by the Central Administration of Health and its suborganizations. Each society has to register with the Central Health Organization of the province or land in which the society has its principal place of business. The order also authorizes the president of the German Administration of Health in the Soviet zone of occupation to organize a scientific medical society of specialists at the medical faculty of the University of Berlin and to call conferences and meetings of specialists in the zone. The agenda of such conferences and meetings has to be submitted for approval to the head of the department of the Central Administration of Health, which has jurisdiction over the matter, at least two months ahead of time.

Attached to the order is the text of the by-laws for establishment of these societies, obligatory on all societies which are organized pursuant to the order. In article 1 of the obligatory charter, the purposes of these societies are defined as follows: the promotion of exchange of research in scientific and practical medicine; the promotion of specialized knowledge; the democratization of the German medical science and of the whole scope of medicine and the uncovering of fascist ideologies within the field of medicine and their complete extermination.

Rehabilitation of the Physically Impaired

On Sept. 10, 1947 a meeting of the Zonal Council of Committees for the Rehabilitation of the Physically Impaired took place in Goslar (British zone). These committees consist of representatives of public health and public welfare, specialists in orthopedics and qualified orthopedic mechanics. All problems of aid to the physically impaired, particularly to war veterans, were discussed. Through the zonal council, the securing of materials to make artificial limbs, the necessary business transactions and the distribution of the materials to orthopedic shops and plants will be coordinated in order to make the amputees independent within the shortest possible time. The committees will also arrange for and supervise professional reeducation. Two rehabilitation schools, in Pyrmont and in Malente, are already in operation. More are to follow.

Miscellany

SOCIAL HYGIENE IN THE FORT KNOX EXPERIMENT

More than a year ago the Army established at Fort Knox, Kentucky, a pilot model of universal military training. As Major Gen. John M. Devine has pointed out, the Army realized that the training of young men involves much more than eight hours a day in technical military training; it must assume responsibility for behavior standards and moral welfare. The experimental unit at Fort Knox has been in operation more than a year and about 1,300 young men have completed training. Only 5 cases of venereal disease, 2 of them in married men who contracted the infection from their wives, have developed; yet there is no prophylaxis station in the unit and no issue of prophylactic kits.

Two periods in the training program are devoted to sex hygiene, each being a cooperative effort by the physician and the chaplain. The physician, who speaks to the trainees first, reveals the normal functions of the human body, treats sex in a matter of fact manner and discusses the symptoms and after-effects of venereal disease. His instruction emphasizes continence as the only sure preventive of venereal disease.

The chaplain takes up the instruction, discussing the moral law, the dignity of women and their function in the reproduction of the race. His discussion also is matter of fact, open, honest, intelligent and frank. These two periods constitute the whole course in sex hygiene; however, the chaplain is available for consultation with individuals at any time and further group instruction is given if he thinks it is desirable.

Sex instruction comprises only a minor part of the social hygiene program. Adequate athletic facilities exist, and six hours a week are devoted to physical training, two to body building and the other hours to instruction on how to play games. Half of this group of typical American boys did not know the basic rules of any team sport, and 10 per cent of them had never played any team game of any kind. The competitive games are carried at the lowest practical level. Competitive athletics which take place every Saturday afternoon have been surprisingly successful in keeping boys in camp over the weekend. Citizens of Louisville and Elizabethtown have invited trainees to their homes and have done a magnificent job in providing and chaperoning young ladies for dances. After four weeks of training in camp, trainees may, under certain conditions, go to town, but they must stay at the Service Club or at an approved home. Although Louisville is "wet" it is an offense in Kentucky, as in most states, to sell liquor to minors and all trainees wear an identifying patch which shows that they are under 21 years of age. Letters were written to every bartender in the city asking them not to sell liquor to any one who wears this patch because that person is a minor. The bartenders have cooperated in this respect.

The most important step in the social hygiene program is the general attempt to raise the moral tone of the organization, to establish standards of behavior and manners that will be a credit to the unit, to encourage the decent against the indecent and the good against the bad. In summary of the program the general said that all this is based on the warm belief that the average American boy of 18 is essentially sound, that he is instinctively decent and that he will do the right thing if he knows what it is.

Medical Motion Pictures

FILM REVIEW

Occupational Health Problems. 16 mm., color, sound, 1,500 feet (one reel), showing time thirty-eight minutes. Prepared in 1947 in cooperation with the American Association of Industrial Physicians and surgeons, Brooklyn Industrial Health Committee, Industrial Health Service of Brooklyn Tuberculosis and Health Association, and others through a grant for instruction by the DeVilbiss Company. Producedbyandprocurable from the Medical Film Guild, 167 West Fifty-Seventh Street, New York 19.

As the film opens, the narrator begins to talk while the observer is trying to read titles. One is impressed that, due to the lack of proper health supervision, over 400,000 man days are lost each year in industry and one-fifth are preventable. The following subjects are included: (1) the penny plan for health education in industry; (2) the technic of preemployment examination; (3) technic of tuberculosis surveys; (4) aerosol therapy and asthma; (5) nutrition in industry; (6) treatment of the common cold; (7) absenteeism in industry; (8) treatment of burns, and (9) industrial hygiene problems. This last phase of the film was produced under the direction of the Department of Industrial Hygiene, State of Illinois., using typical problems created by Chicago's industrial plants. (10) Comparative costs of an industrial hygiene department versus that resulting from compensation. This demonstrates some of the advantages of an industrial health program.

In one scene the right hand of a patient is shown; however, the narrator states "this left hand was caught in a machine." The film has a number of good points. Its general conception of the scope and nature of occupational health is sound, although more dramatic presentation might have been used. Much of the early footage is given over to charts and similar details; however, there is not sufficient time to digest this material. The photography is excellent, particulary those sections on treatment of burns and of asthma which, although they reflect the sponsor's interest, are not distinctively occupational health problems. The film is not regarded as up to professional levels. It might be quite useful as a general introduction to those who are not familiar with the subject.

Abdominal Tube Pedicle Graft to Lower Extremity via Wrist. 16 mm., color, silent, 500 feet (one reel), showing time twenty minutes. Prepared in 1947 by, and procurable on loan from, George A. Friedman, M.D., 111 East Sixthy-First Street, New York 21.

The purpose of this motion picture is to clarify a grafting operation. It illustrates the formation, migration and inlay of the abdominal tube pedicle. The film utilizes motion and still inserts to record the shifting of tubed pedicle flaps from the body to the arm and then to the lower extremity. The contents of this picture comprise a composite of many cases, emphasis being placed on procedure rather than on a single case. In one patient a lesion which is somewhat difficult to make out is shown and one or two immediate final stages are illustrated. Generally speaking, the photography is poor. Several colored still photographs have been copied and interspersed throughout the film. The titles are clear. This production could be shown to audiences unversed in plastic surgery to illustrate one of the more tedious processes required.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1937 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted.

American Journal of Diseases of Children, Chicago

74:657-786 (Dec.) 1947

*Relation of Lesions of Tongue in Children to Niacin Deficiency: H. Bakwin, H. S. Reardon, J. S. Winn and others.—p. 657.
Basal Metabolism of Children with Tumors. Anne Topper.—p. 669.
Hyperosmolarity and Hyperelectrolytemia in Pathologic Conditions of Childhood. S. Rapoport.—p. 682.
Comparison of Axillar and Intraperitoneal Inoculation with Calmette-Guerin Vaccine. Y. Yamaoka and K. Okayasu.—p. 703.
*Gonococcic Vaginitis in Children Treated with Single Injection of Penicillin in Beeswax and Peanut Oil: Report of 20 Cases. B. G. Clarke and H. H. Eisenberg.—p. 707.
Scarlet Fever Immunization: Report on Reversal of Reactions to Dick Test Through Use of New Type of Antigen. Lavinia G. MacKaye and E. H. Watson.—p. 711.
Aid to Interpretation of Changes in Cerebrospinal Fluid in Pediatric Cases. K. H. Beck and B. P. Clark.—p. 714.
Serum Iron Levels in Adolescent Girls: Study of 3 Cases. Frances A. Johnston.—p. 716.

Tongue Lesions and Niacin Deficiency.—From 1942 to 1945 60 children with lesions of the tongue were observed at Bellevue Hospital by Bakwin and his associates. Four types of lesions were observed: acute glossitis; glossitis migrans, or geographic tongue; mild swelling of the tongue, and fissures of the tongue. Effect of large doses of niacinamide (nicotinamide U.S.P.) (8 to 20 mg. per kilogram of body weight) were studied, and results were compared with those for an untreated group. Acute glossitides improved spontaneously or after chemotherapy. Of the patients with swollen and fissured tongues who were treated with niacin (nicotinic acid U.S.P.) a larger proportion showed improvement (14 of 17) than was observed among patients who received no therapy (4 of 16). In no patient was complete cure effected, although treatment was continued in 2 patients for twenty-six months. Glossitis migrans was unaffected by nicotinamide therapy. Diets of children with changes of the tongue were not demonstrably different from the diets of children without such changes. Results support the view that nicotinic acid has a favorable influence on the nutrition of the tongue. They fail to substantiate the view that the lesions of the tongue commonly seen in children are due to nicotinic acid deficiency.

Penicillin in Gonococcic Vaginitis.—Clarke and Eisenberg treated 20 Negro girls from 2 to 10 years of age, who had uncomplicated, previously untreated gonococcic vaginitis, at the Chicago Municipal Social Hygiene Clinic. Purulent or mucopurulent vulvovaginal exudate was present in each patient with local inflammatory signs of varying degree. At least one smear of the vaginal secretion showed typical gram-negative intracellular diplococci before treatment. Children were treated with a single intramuscular injection of 100,000 or 200,000 units of penicillin in beeswax and peanut oil, with prompt clinical and bacteriologic remission in each case. An apparent recurrence after one hundred and twenty-two days, cured by retreatment, was considered to be a reinfection. Untoward reactions to treatment were not observed.

Archives of Pathology, Chicago

44:563-676 (Dec.) 1947

Quantitative Estimation of Fibrous Tissue in Pathologic Livers. S. Warren and P. N. Wahi.—p. 563.
*Preinvasive Carcinoma of Cervix Uteri: Seven Cases in Which It Was Detected by Examination of Routine Endocervical Smears. E. R. Pund, H. E. Nieburgs, J. B. Nettles and J. D. Caldwell.—p. 571.
Rare Anomaly of Vermiform Appendix: Mucous Lining of External Surface. S. Mahrburg.—p. 578.
Primary Atypical Pneumonia: Report of 8 Cases with Autopsies. F. Parker Jr., L. S. Jolliffe and M. Finland.—p. 581.
Intra-Articular Changes Induced in Rabbits by Injection of Typhoid Somatic Antigen. H. R. Morgan and G. A. Bennett.—p. 609.
*Fibrosis Uteri. R. Shoemaker and J. E. Kahler.—p. 621.
Parathyroid Adenoma with Generalized Metastatic Calcification. M. O. Young and B. Halpert.—p. 628.
Reticuloendothelial Cells Reacting to Toxic Antigens and to Infection. P. Bueno.—p. 635.
Nucleolar Substance in Anterior Lobe of Human Pituitary Gland. C. Cavallero.—p. 639.
Improved Method for Handling Photolabile Liquids. J. Nichols.—p. 646.

Detection of Preinvasive Carcinoma by Smears.—According to Pund and his associates incipient cancer of the cervix uteri is usually noninvasive. Adequate therapy in this phase should result in cure in 100 per cent of the cases. The endocervical smear stained according to the method of Papanicolaou offers the best routine method of detecting neoplastic cells of the cervix in their preinvasive phase. The diagnosis must be confirmed by biopsy or endocervical curettage. A study of routine endocervical smears has enabled the authors to detect 7 cases. Biopsy of two or more sites should be carried out, exercising care to choose the proper sites—the endocervical junction at the external os.

Fibrosis Uteri.—Shoemaker and Kahler point out that the criteria for the diagnosis of fibrosis uteri have never been clearly defined and its existence as a separate entity has been denied by some. The surgeon who has made a preoperative diagnosis of uterine myoma or adenomyosis may encounter at operation a symmetric, slightly enlarged uterus. This type of uterus gives rise to menorrhagia. In order to determine whether the disease is a clinical entity, fresh uteri received from the surgery division were inspected, measured and opened along the middle of the anterior surface. The organ was then halved by continuing the incision, and a block of tissue was removed to represent the full width of the uterus. Twenty-seven uteri with fibrosis and 28 control uteri were studied. The control group consisted of necropsy and surgical specimens which were normal or contained leiomyomas, adenomyosis or endometrial polyps. The 27 cases of fibrosis uteri were found among a total of 245 uteri. The patient with fibrosis uteri has a history of profuse menorrhagia without metrorrhagia and usually without dysmenorrhea. On pelvic examination the uterus is symmetrically enlarged. The excised uterus is a slightly to moderately enlarged organ. The myometrium is pale, finely textured and thickened, with increased consistency. On microscopic examination an increase of fibrous tissue is observed in the submucous layer of the myometrium, appearing as an increase of both the interfascicular and the intrafascicular connective tissue. This study does not reveal the exact causation or pathogenesis of the lesion but does provide evidence that it is not an end stage of chronic metritis, that hypertrophy of muscle fibers plays a minor role and that it is not a form of subinvolution of the uterus. The authors conclude that fibrosis uteri may be considered a fairly well delimited clinical and pathologic entity. The lesion consists of fibrosis of the myometrium.

Archives of Physical Medicine, Chicago

29:1-58 (Jan.) 1948

Medical Research. A. C. Ivy.—p. 7.
Studies Concerning Effect of Deep Tissue Heat on Blood Flow. C. H. Kemp, W. D. Paul and H. M. Hines.—p. 12.

Effect of Diathermy on Blood Flow: Plethysmographic Studies. C. S. Wise.—p. 17.
*New Devices for Disability Evaluation: I. Hand, Wrist, Radioulnar, Elbow and Shoulder Ergographs. F. A. Hellebrandt, Helen V. Skowlund and L. E. A. Kelso.—p. 21.
Dynamic Aspects of Physical Medicine in Veterans Administration. A. B. C. Knudson.—p. 29.
Biologic and Physiologic Effects of Ultraviolet Radiation. E. E. Gordon.—p. 36.
Tracing Device for Surface Lesions. L. B. Newman.—p. 42.

Evaluation of Disability.—Hellebrandt and associates state that the upper extremities are used in nearly all occupational pursuits. Deformities, injury or disease affecting the power of the muscles reduce man's ability to work. When this occurs grave economic problems related to the adjudication of compensation claims arise. A series of self-contained, ink-writing ergographs have been developed for the appraisal of the functional capacity of the major articulations of the upper extremity. Preliminary trial with these instruments suggests that work tolerance may be estimated with greater accuracy ergographically than by judgment of the examining physician and that ergography may be clinically useful in disability evaluation, because it provides a simple quantitative tool by virtue of which the following measurements may be made: (1) initial functional capacity; (2) progress under treatment; (3) the end point of effective rehabilitation, and (4) the degree of residual disability.

Arkansas Medical Society Journal, Fort Smith

44:181-198 (Jan.) 1948

Cancer of Stomach. J. D. Hayes.—p. 181.
*Tularemia in Arkansas. R. H. Rigdon and C. R. Chesnutt Jr.—p. 183.

Tularemia in Arkansas.—Rigdon and Chesnutt review 26 cases of tularemia at the University Hospital in Little Rock from 1940 to 1946. There were 18 cases of the ulceroglandular type, 3 of the pneumonic form and 2 each of the oculoglandular and typhoid types; 1 case was unclassified. Cases are presented to illustrate each of the four types of infection. In most of the cases treatment was with sulfonamide drugs. Now streptomycin is the drug of choice in the treatment of tularemia.

Bulletin of Johns Hopkins Hospital, Baltimore

82:1-80 (Jan.) 1948

*An Anti-Rh Antigen-Antibody Reaction Factor (the Rh Protective Factor): Preliminary Report. A. Bloxsom and Rose Matthaei.—p. 1.
Psychotherapy in General Medical Practice. J. C. Whitehorn.—p. 10.
Resistance of Young Rabbit to Diabetogenic Effect of Alloxan. C. S. Schultz and J. R. Duke.—p. 20.
Malignant Tumors of Nasopharynx. T. E. Van Metre Jr.—p. 42.
*Treatment of Miliary Tuberculosis with Promizole. Edith M. Lincoln, S. Stone and Olga R. Hoffman.—p. 56.

Rh Protective Factor.—Bloxsom and Matthaei reported in an earlier article an infant with erythroblastosis fetalis who accidentally received a massive transfusion of Rh-negative blood. Since the course of the hemolytic disease of this infant was favorably altered by the large transfusion, the possibility was suggested that an Rh-negative donor's serum might possess some factor that suppressed or inhibited the Rh antigen-antibody reaction. If this is true, the serum of Rh-negative donors should be of as much value in transfusions into infants with erythroblastosis fetalis as the Rh-negative red blood cells. The present study was undertaken to determine whether this factor could be demonstrated in Rh-negative blood serums. The serums of the Rh-negative bloods employed in these studies have been shown to contain an anti-Rh antigen-antibody reaction factor that inhibits the Rh antigen-antibody reaction. The serums of the Rh-positive bloods have been shown to contain no anti-Rh antigen-antibody reaction factor except for the small amount found in one man who is heterozygous. This anti-Rh antigen-antibody reaction factor is a specific inhibiting substance for the Rh reaction. The natural occurrence of this anti-Rh antigen-antibody reaction factor serves as a vital protective means for Rh-negative persons and for infants subject to hemolytic disease of the newborn. It is believed that the serum of Rh-negative blood is probably even more valuable than its cells for the transfusion of infants with erythroblastosis fetalis due to anti-Rh agglutinins. The males tested showed in their blood serums greater amounts of this anti-Rh antigen-antibody reaction factor. It is possible that blood from such donors will be more effective in the treatment of hemolytic disease of the newborn. It is hoped that the use of suitable Rh-negative blood and blood serums at regular intervals before delivery may result in the salvage of a larger number of those infants. The presence of the anti-Rh antigen-antibody reaction factor in the serums of Rh-positive males may point to the fact that those males are heterozygous.

"Promizole" in Miliary Tuberculosis.—Lincoln and his associates tried "promizole" (4,2'-diaminophenyl-5'-thiazolylsulfone) first in that form of tuberculosis which has the worst prognosis. They treated 5 successive patients with meningitis without beneficial effects. Acute generalized hematogenous tuberculosis was then selected for treatment with the drug because the course of this disease is more prolonged than that of meningitis, thus allowing more time for action of a drug. The authors have employed "promizole" in 11 children with acute miliary tuberculosis. All showed evidence of primary pulmonary tuberculosis as well as mottling of miliary or slightly larger size throughout both pulmonary fields. Three of these patients have been treated for less than six months, and although all are doing well it is too early to evaluate results of therapy. Three patients were treated for less than a month. Five consecutive patients with acute generalized miliary tuberculosis were apparently adequately treated with "promizole." Of these, 2 children died forty-three days and four and one half months, respectively, after therapy was begun. Three children showed complete recession of roentgenologic evidence of miliary tuberculosis and are alive thirty to thirty-three months after the drug was first given. In these patients who survived acute miliary tuberculosis the primary pulmonary lesions cleared slowly and in 2 cases went on to cavitation. In 1 case roentgen evidence of the primary focus is still present. One child developed tuberculosis of the spine, choroiditis and positive urine cultures for tubercle bacilli while taking the drug. All 3 patients are still receiving maintenance doses of "promizole." The drug is goitrogenic and has a stimulating effect on secondary sexual characteristics, causing enlargement of nipples and mammary tissue and growth of pubic hair. Toxic effects which would require permanent discontinuance of the drug were not observed.

California Medicine, San Francisco

68:1-56 (Jan.) 1948

Bleeding Nipple as Diagnostic and Therapeutic Problem. I. MacDonald.—p. 1.
Painful Breast. J. M. Neil.—p. 5.
Diagnosis of Early Breast Cancer. W. D. McCarthy.—p. 7.
Place of Radiation Therapy in Management of Breast Cancer. L. S. Goin.—p. 11.
Management of Inoperable Cancer of Breast. E. Reynolds.—p. 14.
Rural Medical Care and Hospitalization. C. B. Andrews.—p. 16.
Oral Substitution Therapy with Benzestrol for Patients with Estrogen Deficiency. F. E. Harding.—p. 20.
"Warts". H. J. Templeton.—p. 23.
Overlooked Foreign Body in Tracheobronchial Tree: Case Report. M. E. Childress, P. C. Samson and D. J. Dugan.—p. 25.
Ureteral Reflux. J. Steinberg.—p. 27.
*Leukonychia. D. W. Montgomery.—p. 29.
Does Milk "Make Mucus"? R. M. Moose.—p. 31.
Further Study of Pneumonia in San Francisco, 1944-1946. G. F. Warner and F. H. Gardner.—p. 32.
Cause for Reestablishment of Communication Following Ligation of Patent Ductus Arteriosus. C. E. Rees.—p. 35.
Cancer of Lip. I. MacDonald.—p. 37.

Radiation in Cancer of the Breast.—According to Goin, clinical stage 1 cancer of breast means that the tumor seems to be limited to a lobule of mammary tissue, that the skin is uninvolved and that no axillary or supraclavicular nodes are palpable. Pathologic stage 1 means that no carcinomatous cells could be found in the tissue removed. Clinical stage 2 carcinoma means that the skin is involved or that palpable nodes are present, or both. Pathologic stage 2 means that the skin was infiltrated or that metastases to glands were demonstrated, or both. Stage 3 cancer of the breast indicates the presence of distant metastases. The author thinks that stage 1 mammary carcinoma should not be irradiated but should be treated by radical mastectomy. Stage 3 carcinoma of the breast should be

treated entirely with irradiation. Stage 2 cancer of the breast should be treated by radical mastectomy plus postoperative irradiation. There is little to lose and perhaps much to gain by the castration of menstruating women who have cancer of the breast.

Leukonychia.—Montgomery points out that white spots on the nails are especially frequent in young women and are observed more frequently on the fingers than on the toes. Injury, particularly that incident to manicuring, may play a part in the development of some of the white spots and streaks. They may occur as the result of severe fever. White stripes or cross ridges have been observed corresponding to severe attacks of typhoid or typhus or other fevers, and 1 case has been reported in which each attack of relapsing fever was followed by a leukonychia stripe. Nerve lesions may cause white stripes on the nails; they are frequent in the neurotic person; they concur with constipation, indigestion and acne, and they may have some connection with the menstrual period. Poisons such as arsenic or alcohol may play a part in the development of white spots and stripes in the nails. Often leukonychia indicates a more or less grave, persistent state of ill health.

Journal of Nutrition, Philadelphia

34:603-766 (Dec.) 1947. **Partial Index**

Observations on Beef Cattle Affected with Generalized Edema or Anasarca Due to Vitamin A Deficiency. L. L. Madsen and I. P. Earle. —p. 603.

Nutritive Value of Canned Foods: XXV. Vitamin Content of Canned Fish Products. J. B. Neilands, F. M. Strong and C. A. Elvehjem. —p. 633.

Influence of Pteroylglutamic Acid (Member of Vitamin M Group) on Gastrointestinal Defects in Sprue: Study of Interrelationships of Dietary Essentials. W. J. Darby, E. Jones, H. F. Warden and Margaret M. Kaser.—p. 645.

*Effects of Caloric Restriction on Skeletal Growth. P. Handler, G. J. Baylin and R. H. Follis Jr.—p. 677.

*Effect of Added Thiamine on Growth, Vision and Learning, Using Identical Twins. E. C. Robertson, C. M. Tatham, Norma F. Walker and M. R. Weaver.—p. 691.

Nutritional Studies on Milk Fat: III. Effect of Treatment of Milk Fat with Certain Solvents on Growth of Young Rats. E. L. Jack and E. B. Hinshaw.—p. 715.

Caloric Restriction and Skeletal Growth.—Handler and his co-workers found that the rate of skeletal growth in young rats was roughly proportional to the rate of general body growth when caloric restriction was the factor limiting growth. Restriction of caloric intake to about one half of that of control animals fed ad libitum resulted in a complete cessation of both skeletal and generalized body growth. Histologically the bones of such animals were identical with those usually found in "partial inanition." In larger, not quite completely grown rats, caloric restriction sufficient to cause a loss of 40 per cent of their initial body weight only slightly decreased the rate of skeletal growth. The plasma concentration of calcium was normal in all animals, while that of inorganic phosphate was below normal in the young caloric-restricted animals but not in the older rats.

Effect of Added Thiamine in Twins.—Robertson and his associates found that administration of 2 mg. daily of thiamine for four and one-half months to half of thirty-six pairs of identical twins resulted in improvement in weight and height gains and in manual dexterity and prolonged memory test scores that were of questionable statistical significance. The tests used for measuring vision, intelligence, reasoning, arithmetic, rote memory and code substitution gave results without statistical significance. Twenty-five pairs of the twins were kept in the study for four and one-half months longer. When they were again tested at the end of this period, that is, after nine months of therapy, no gains of statistical significance were evident in any of the tests.

Review of Gastroenterology, New York

15:1-100 (Jan.) 1948

Diagnosis of Prepyloric Lesions in Stomach. H. A. Osgood.—p. 11.

*Experience with Papanicolaou Stains of Gastric Contents. J. P. Campbell and H. A. Grimm.—p. 21.

Some Observations on Effect of Synthetic Folic Acid on Alimentary Tract of Patients with Tropical Sprue. F. Milanes, T. D. Spies, R. H. Beguerie and G. G. Lopez.—p. 33.

Teaching Comprehensive Gastroenterology. G. S. Stevenson.—p. 44.

Chronic Focal Infection—Gastroenterologic Problem. J. W. Wiltsie. —p. 50.

Carcinoma of Large Intestine. Review of Personal Experience in Private Practice. A. O. Wilensky.—p. 55.

Papanicolaou Stains for Gastric Contents.—Campbell and Grimm studied the cell structure of gastric contents by means of the Papanicolaou method of preparing and staining slides. Gastric contents of 200 patients were examined; 28 had gastric, duodenal or gastrojejunal ulcers; 2 had pernicious anemia; 1 had gastric polyps; 1 had carcinoma of the pancreas; 3 had disease of the biliary tract; 7 had carcinoma of the stomach, while the balance were controls or patients with disease of the lower part of the gastrointestinal tract. The authors realize that the possibilities of this method for detecting or at least suspecting early gastric carcinoma cannot be completely determined without the lapse of more time to follow up the patients covered in this study. A subsequent comparison of slides of their gastric contents with those now on hand, especially in those that later have cancer of the stomach, will be necessary. The Papanicolaou stained smear offers promise of confirming a diagnosis of cancer of the stomach in cases in which the lesion has advanced to the point where it can be diagnosed by roentgen ray. Of 5 cases of carcinoma of the stomach in which the authors were able to obtain the surgical or autopsy specimen, they were able to demonstrate cancer cells in 4. Cancer cells were found in 1 of 2 patients in whom the diagnosis had been established clinically; the other case was one of linitis plastica, in which a study of the gastric contents may never be productive. The Papanicolaou stained smear of gastric contents is a relatively simple procedure. It is inexpensive to conduct. It is adaptable to studying large numbers of patients with a minimum of inconvenience and expense.

Urologic & Cutaneous Review, West Palm Beach, Fla.

51:621-668 (Nov.) 1947

Parageusia as Symptom of Genitourinary Disease. B. S. Abeshouse and S. Lerman.—p. 621.

Urinary Incontinence Following Transurethral Resection with Special Reference to Nonsurgical Treatment. J. A. Lazarus and M. S. Marks. —p. 626.

Management of Azotemia Due to Obstructive Calculous Disease. C. P. Mathe.—p. 630.

Vulvitis Due to Stress Urinary Incontinence. J. W. Davies.—p. 635.

Lower Nephron Nephrosis: Complication of Transurethral Prostatic Resection. S. S. Baird and H. M. Spence.—p. 642.

Unusual Primary Urethral Calculus: Case Report. C. S. Fromm.—p. 646.

Metastatic Retroperitoneal Tumor from Undescended Testicle. J. I. Farrell and R. L. Atkinson.—p. 646.

Delayed Nephrectomy in Acute Stone Pyonephrosis. H. A. Levin. —p. 648.

Contribution to Etiology, Diagnosis and Therapy of Pemphigus. D. I. Macht and M. Ostro.—p. 651.

Etiology, Diagnosis and Therapy of Pemphigus.—According to Macht and Ostro, the blood serum of patients with true pemphigus exhibits a specific phytotoxicity on the root growth of Lupinus albus seedlings, which is not exhibited by the serums of most other dermatoses (Pels-Macht or Macht-Pels test). This toxic reaction of the serum of patients with pemphigus is diminished or completely destroyed by exposure to specially filtered roentgen rays, while serums from patients with other dermatoses are not affected by such rays (Macht-Ostro reaction). The two tests performed simultaneously lead to a reliable differential diagnosis of pemphigus. As suggested by these observations, deep roentgen irradiation was performed on 10 patients, 6 men and 3 women between the ages of 45 and 68 and 1 young woman with pemphigus. The rays were filtered through 1 mm. aluminum and 2 mm. copper. The dosage varied from 43 r to 86 r measured in air. A rest period of two or three days was usually given between each treatment and seldom were more than three treatments made in close succession. Detoxification of the blood serums of all patients resulted as determined by the phytopharmacologic test. This was accompanied by definite clinical improvement and remission in 7 of the patients with a permanent remission or cure in 2. The young women with fulminating pemphigus vulgaris and 1 middle-aged man with pemphigus foliaceus did not improve clinically and died. A third patient with extensive pemphigus vulgaris showed some slight clinical improvement but is now rapidly approaching the end. The last 2 patients were treated with rays filtered not through 2 mm. copper but through 0.5 mm. copper. Further investigation of the clinical therapeutic possibilities of radiotherapy for pemphigus as checked or controlled by phytopharmacologic tests is suggested.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Radiology, London

20:489-540 (Dec.) 1947. Partial Index

Symposium on Carcinoma of Stomach:
Carcinoma of Stomach: A Radiologist's Point of View. J. L. A. Grout.—p. 491.
Gastroscopy in Diagnosis of Gastric Cancer. H. W. Rodgers.—p. 502.
Cancer of Stomach: Some Pathologic Considerations. M. J. Stewart. —p. 505.
Surgical Aspect of Carcinoma of Stomach. H. Taylor.—p. 507.
Association of Achalasia of Cardia with Esophageal Carcinoma. P. Baer and K. Sicher.—p. 528.

Edinburgh Medical Journal

54:529-592 (Oct.) 1947. Partial Index

Vagotomy in Treatment of Peptic Ulcer. C. F. W. Illingworth and A. W. Kay.—p. 540.
Anatomic Evaluation of Operations for Hypertension. G. A. G. Mitchell. —p. 545.
Some Results in Treatment of Lupus Vulgaris by Calciferol. T. E. Anderson.—p. 562.
Prognosis in Pulmonary Tuberculosis. R. Fraser.—p. 566.

Evaluation of Operations for Hypertension.—Mitchell says that although the cause of hypertension is uncertain, the main surgical attack has been directed against peripheral sympathetic structures. To cover various etiologic possibilities a blunderbuss technic has been evolved requiring extensive autonomic ablations. Different surgeons have differing ideas about what they wish to achieve, and these varying views are reflected in their operations. Nearly all wish to produce vasodilatation in the abdominal splanchnic area, and in addition most believe that a degree of somatic vasodilatation is desirable. The author reviews various types of operations and suggests that certain of the failures may be explained on anatomic grounds. It is shown that the Peet, Allen-Adson and Smithwick procedures may not interrupt all the sympathetic fibers to the abdominal splanchnic area or to the kidneys and adrenals. Aortic and esophageal filaments arising from the sympathetic trunks or splanchnic nerves above the levels of section, paraaortic nerves (when present) and sympathetic fibers in the phrenic nerves, esophageal plexuses or vagal trunks may all reach the abdomen and may escape interruption in these sympathectomies. Section at the level of the second lumbar ganglion may miss renal contributions arising from the sympathetic trunks below that level and may not interrupt communicating fibers between the renal plexus and the superior spermatic, gastroduodenal or intermesenteric nerves. It is suggested that the optimum sympathectomy for hypertension is bilateral resection of the sympathetic trunks from the fourth thoracic ganglion to the third lumbar ganglion and removal of the splanchnic nerves.

Calciferol in Lupus Vulgaris.—Anderson says that in the past year 71 cases of lupus vulgaris (19 males and 52 females) have been treated with calciferol (vitamin D_2) at the Aberdeen Royal Infirmary. Eighteen of the patients are either still undergoing treatment or have defaulted. One patient died. In this patient calciferol treatment had been interrupted on account of toxic symptoms. A course of treatment has been completed in 52 of the patients. Of these, 41 were apparently cured and 8 were greatly improved but doubtful; the remaining 3 were apparently cured at the end of a six months' course of treatment but are relapsing and require further treatment. Calciferol was the exclusive treatment in 39 of the 52 patients; in the other 13 some adjuvant treatment was used, such as intradermal chaulmoogra oil esters, carbon dioxide snow or the Kromayer lamp. The duration of calciferol treatment varied from two and one half to eight months (average, 6.1 months). The usual dosage of calciferol was 50,000 international units three times daily by mouth in cases in which this dosage was tolerated. In most cases this has been reduced to 100,000 units a day after three months, but in some instances 150,000 units have been administered daily for a full six months. A rise of the serum phosphate level seems to be a more reliable index to early intoxication than the calcium level. Toxic symptoms appeared in 32 of the patients, but subsided. The results obtained with calciferol are superior to those formerly obtained by other methods.

Revue Neurologique, Paris

79:481-560 (July) 1947

Special Intermediary Type Between Thomsen's Disease and Myopathia; Contribution to Study of True Muscular Hypertrophy in Progressive Muscular Dystrophia. L. Rouques, P. Guilly, J. Pautrat and J. Lapresle.—p. 481.
*Vegetative Hypertrophic and Atrophic Sciatic Neuralgia. V. Pitha. —p. 491.

Vegetative Sciatic Neuralgia.—Pitha reports 15 cases of vegetative hypertrophic and atrophic sciatic neuralgia, a syndrome associated with hernia of the intervertebral disk and classic funicular sciatica and with certain cases of the Guillain-Barré syndrome and neuritis. This vegetative sciatic neuralgia of rheumatic origin is to be considered a new clinical entity different from that of classic sciatica (Cotugno's disease). This atrophic and hypertrophic sciatica is characterized by a certain type of pain. Except for the initial dramatic attack of pain, it is relatively mild, always tolerable, sometimes burning and occasionally diffuse, particularly in the area of the calf. The muscle group involved is severely and diffusely painful on palpation, in contrast to a mild or absent Lasègue's sign. In the initial acute stage of the disease there may be present occasionally the classic signs of sciatic radiculitis, and the term "total neuralgic phase of vegetative sciatica" is suggested for it; the hypertrophic type may often be associated with intense pain in the lumbar region and in the abdomen. The muscular changes occur slowly after the acute stage, and they characterize the chronic stage. There are no real disturbances of motility, and muscular weakness may occur only after a prolonged walk. The muscular changes are diffuse and involve the entire limb. The upper half of the calf is particularly affected, and hypertrophy of the thigh may be associated with atrophy of the leg in the same patient. There are no fibrillary tremors. The muscle tonus is increased in the hypertrophic form and diminished in the atrophic form. The idiomuscular excitability is mildly and regularly diminished in the hypertrophic and in the atrophic sciatica. In general there are no changes in the tendon reflexes in both forms. The course of the atrophy is a slow one, sometimes of several years' duration, but the hypertrophic form develops in several months. These muscular symptoms are to be considered as the most important clinical aspect of the direct vegetative innervation of muscles. It may be safer to explain the common sciatic changes on the basis of a vegetative pathogenesis of the muscular changes than on one of inactivity.

Wiener medizinische Wochenschrift, Vienna

97:533-556 (Dec. 20) 1947. Partial Index

Determination of QT Interval in Electrocardiogram. W. Wolf.—p. 533.
*Problem of Decapsulation of Kidneys in Acute Anuresis. W. Pilgerstorfer.—p. 535.

Decapsulation of Kidneys in Anuresis.—Pilgerstorfer treated 1 man aged 23, who had acute nephritis associated with anuresis, by unilateral removal of the renal capsule. Previous conservative treatment consisting of two days of fast and then a diet of dried, uncooked fruits. Intravenous injections of strophanthin and dextrose and short wave radiation had proved ineffective in promoting the secretion of urine. Considerable amounts of urine were passed within a few hours after the surgical intervention. In seven postoperative days the secretion of urine amounted to about 34 liters, 14 of which were excreted in the first thirty-six hours. Simultaneously the residual nitrogen, which before the operation had been increased to 197.4 mg. per hundred cubic centimeters, was restored to normal as were the blood pressure, the specific gravity of the urine and the function of the kidneys. The lightning, lifesaving result of the unilateral decapsulation in this case suggests that the operation should be performed in cases of acute nephritis in which, in the absence of severe histologic changes in the glomeruli, anuresis may result from the mechanical compression of the highly edematous kidney by the tight capsule. The liberation of the kidney from the compressing capsule may be compared to the flood of water which has been dammed up in a reservoir and which pours out after the removal of the obstruction. Due to the diuresis resulting in the decapsulated kidney the swelling in the other kidney also subsides and both kidneys resume their function. In contrast to this, diuresis will not take place even from bilateral decapsulation in cases of severe subacute glomerulonephritis associated with extensive extracapillary proliferation.

Book Notices

Viruses. By Max A. Lauffer, Ph.D., Associate Research Professor of Physics, the University of Pittsburgh, Pittsburgh. From the Twentieth Annual Priestly Lectures. Sponsored by Phi Lambda Upsilon Honorary Chemical Society. Paper. Pp. 62, with 42 illustrations. Pennsylvania State College, State College, Pennsylvania, 1946.

This volume contains five chapters which served as the twentieth annual Priestly lectures. The subjects chosen by the author, who is an associate research professor of physics of the University of Pittsburgh, are largely concerned with biophysical properties of certain viruses which have become available in large enough quantities and in states reasonably pure enough to warrant biophysical analyses.

The first lecture deals with "viruses as molecules"; the fourth considers "viruses as organisms." This in itself does not imply a contradiction, since it becomes more and more obvious that a variety of agents are included at present under the heading of viruses. The second and third lectures are entitled "the size and shape of viruses" and "the disintegration of viruses," whereas the last considers "viruses and human welfare."

The experimental data quoted, of which a sizable share involves the author's work, are concerned to a large extent with plant viruses, tobacco mosaic virus in particular, and the influenza viruses. The biophysical apparatus used in the study of the various properties of the agents is briefly described in the corresponding sections, and the theories and limitations of the technics are adequately discussed. Thus it is possible for those less well versed in biophysical technics to follow the line of thought without difficulty, which renders this volume valuable to those interested in the virus field in general.

The last lecture sums up some of the better known facts about the profound influences exerted by virus infections of plants, animals and man on the course of history and man's efforts to overcome these scourges. Some of them have been practically eradicated; other attempts led to encouraging results. Some of these have been overrated by the author, and to link biophysical studies with the conquest of certain virus diseases seems somewhat forced. To quote: "Yet who ever could have dreamed that the crystallization of urease and of pepsin would open the way for the conquest of influenza?"

Practical Obstetrics. By Bruce T. Mayes, M.V.O., M.B., B.S., Professor of Obstetrics, University of Sydney, Sydney. Cloth. Price, 37s. 6d. Pp. 306, with drawings by Vergil Lo Schiavo, B.A. The Australasian Publishing Co., Pty. Ltd., Bradbury House, 55 York St., Sydney, N. S. W.; 182 High Holborn, London, W. C. 1, 1947.

It was the author's intention not to write a textbook but to present a number of practical clinical discussions in a form that will preserve the atmosphere of a doctor's office, an operating room or the bedside rather than that of the lecture hall. In this the author has succeeded admirably, for his style of presentation is delightfully informal and most unusual in a book dealing with medicine. Of the twenty-two chapters in the book, eighteen are devoted to obstetrics, two to sterility, one to artificial insemination and the last one to "Queries and Views."

The first chapter deals with postpartum hemorrhage, and this is proper because hemorrhage is the most important cause of maternal mortality. Throughout the book the author demonstrates his vast experience in obstetrics. He is ultra-conservative, yet he has not failed to accept all that is progressive in obstetrics. He illustrates and describes the use of episiotomy, direct local anesthesia and the low cervical cesarean section. He also takes up the matters of the Rh factor and rubella and their significance in obstetrics.

There are a few recommendations with which many will disagree. These are the Credé expression for the separation of the placenta, intrauterine douches for the control of postpartum hemorrhage and chloroform to relax spasms of an eclamptic convulsion.

The book not only is written in an interesting fashion but is beautifully illustrated by drawings and photographs, many of which are in color. Throughout the book are case reports which greatly enhance its teaching value. This is a real textbook, not only for medical students and general practitioners, for whom it is intended, but also for specialists in obstetrics.

Successful Dental Practice: Patient Relations—Patient Education—Treatment Planning—Business Principles. By J. Lewis Blass, Ph.G., D.D.S., Associate Professor of Periodontia, New York University College of Dentistry, New York, and Irvin Tulkin, D.D.S., Post-Graduate Instructor on Dental Practice Management, First District Dental Society of New York. Twenty drawings by Jean McConnell. Fabrikoid. Price, $6. Pp. 221, with 42 illustrations. J. B. Lippincott Co., 227-231 S. 6th St., Philadelphia 5, 1947.

Untiring effort and much time have gone into the preparation of this book. The authors have presented cogent and well thought out principles and procedures which can be of great assistance to the reader. Although this book is intended particularly for practitioners of dentistry, much of its matter will apply to the practice of medicine. In both professions technical ability is recognized as the foremost reason for success, but a host of other factors influence each particular practice. The solutions to various problems which this book offers are based on the experience of successful practitioners.

The book is divided into five parts. Part 1, "patient relations," presents attitudes and procedures helpful in securing effective relations with patients. Receiving the patient, educating the patient during the examination, planning and presenting the diagnosis, outline of treatment, fees and terms are discussed in detail. Particularly interesting and instructive is the portrayal of conversational technics for meeting the problems of the patient in the initial interview. These problems pertain principally to fees, fear of pain, prejudices and misconceptions or ignorance. The vast importance of creating and maintaining the confidence of the patient is emphasized throughout the chapter.

"Office Management" is the title of Part 2. The authors present a comprehensive study of fee arrangements, bank loans, credit and collections, office responsibilities, secretary's duties, records, practice control and correspondence. Emphasis is placed on retaining the patient's good will.

Part 3 covers "Insurance and Legal Considerations and Personal and Psychologic Considerations." This section is the most valuable part of the book. The observations quoted from Charles H. Kendall on the "value of psychology to the dentist both in handling his patients and in knowing himself" and the material furnished by Isabelle Beaumont on the "management of the neurotic patient" are well worth the price of the book.

Part 4 is devoted to "Business Considerations," and the recent graduate will find valuable information about various types of practice as well as adequate listings of practice locations. Problems of practice and practice growth are covered thoroughly, and conclusive answers are given to forty-three questions concerning patient relations.

The book concludes with an "Atlas for Patient Education." The publishers are to be commended for the beautiful and distinct illustrations which assiduously conform to the text.

It is impossible in a brief review to supply an adequate idea of the importance of this book, which is characterized by truth and dignity.

Principles of the Contact Lens. By H. Treissman, M.B., B.S., F.R.C.S., and E. A. Plaice. Cloth. Price, $3.50. Pp. 88, with 40 illustrations. The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, 1947.

This small textbook is really a handbook for the guidance of the ophthalmologist in selecting those patients who might wear contact lenses with benefit.

There is an excellent section with clear diagrams on the optics of contact lenses, but the section on indications is neither impartial nor scientific. It is unfortunate that ophthalmologists are rather sharply divided on the question of contact lenses, some being ardent advocates, others being as ardent opponents. The authors clearly belong to the former group, and therefore the indications for use of contact lenses will not be universally accepted.

Sattler's veil, or the fogging of vision which results from corneal edema, is the greatest single problem facing those who work with contact lenses today. The proposed method of solving this problem by simply removing the contact lens and reinserting it a half-hour later is open to severe criticism and entirely unsubstantiated by experience in this country.

On the whole, this handbook is not impartial enough to be a good handbook and is not nearly detailed or explicit enough to be a good source of information on contact lenses.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

INDUCTION OF LABOR

To the Editor:—**Is the use of ergot for induction of labor a recognized and safe procedure? The regimen consists of an enema, 12 grains (0.78 Gm.) half strength powdered ergot by mouth and one hour later 6 grains (0.39 Gm.) of powdered ergot, if uterine contractions have not previously ensued. Artificial rupture of the membranes may be performed also if the fetal head is engaged.**

K. W. Covey, M.D., Mahnomen, Minnesota.

ANSWER.—The oxytocic activity in powdered ergot varies greatly. It is far better to use the active principle of ergot, ergonovine, whenever the action of ergot is desired. There have been some reports in the literature describing the use of small doses of ergonovine for the induction of labor. Generally, however, ergot is not desirable for induction because it has a tendency to induce uterine tetany rather than normal rhythmic contractions.

Induction of labor has become a standardized procedure. The patient should be at or near term. The fetal head should be engaged in the pelvis to decrease the hazard of prolapse of the cord. The cervix should be "ripe"; that is, it should be short, its canal having been largely taken up in the process of effacement, and the cervical os should be soft and patulous, easily admitting one or two fingers. If these conditions are fulfilled the simple rupture of the membranes will be followed by the onset of labor after a latent period of one to six hours. No medication is necessary. Obviously, one should have a medical indication for the induction.

"Pitocin" can be used for induction, but it is rarely necessary. One should start with ½ minim (0.31 cc.) given subcutaneously and increase by ½ minim at fifteen minute intervals until a dose of 3 minims (0.18 cc.) has been reached. Total dose should not exceed 1 cc The patient should be watched carefully. If tetany of the uterus develops the drug should be discontinued. Medication should likewise be stopped when regular uterine contractions begin.

REACTIONS TO TESTS FOR UNDULANT FEVER

To the Editor:—**Dr. A. J. Durant of the University of Missouri, chairman of the Veterinary Science Department, states that "only 4 per cent of the people that are infected react to the blood test for undulant fever, while 96 per cent of the cattle that have the disease react positively and reliably to the test." In a survery by the Indiana State Board of Health of especially exposed groups of persons, 50 per cent of the veterinarians who submitted themselves to the plate agglutination test showed a positive reaction. With fertilizer plant workers the proportion was 27 per cent.**

Is the Indiana State Board of Health, or is Dr. Durant of Missouri in error? Should physicians continue to depend on Missouri laboratory procedure, or should it be discarded and should patients be treated on the basis of their present and past symptoms? The State of Missouri does not make cultures or use guinea pig inoculations for these tests.

Ira Allison, M.D., Springfield, Mo.

ANSWER.—The information cited from either source need not be suspected of being incorrect. With reference to the infected human being the important item of the stage of disease at which the tests were performed has been omitted. If serum agglutination tests are performed but once and at random, without respect to the duration of disease, in a large group of persons exposed to brucellosis for some years the proportion of positive agglutination tests may well be 4 to 5 per cent. In the survey of Gould and Huddleson (Gould, S. E., and Huddleson, J. F.: Diagnostic Methods in Undulant Fever (Brucellosis), with Results of Survey in 8,124 Persons, J. A. M. A. **109**:1971-1974 [Dec. 11] 1937), "of 623 infected persons 33, or 5.3 per cent, gave a positive agglutination test." The interpretation of the word "infected" is also at stake. In the passage cited it apparently carries the meaning of having at any previous time been invaded with brucella, without any implication that such invasion ever resulted in disease; and in the reference cited it means by definition a person who exhibited a positive intradermal test reaction and a low to moderate opsonocytophagic titer.

Since brucellosis can seldom be diagnosed with certainty by either clinical or laboratory criteria alone physicians must continue to use all available evidence, epidemiologic, clinical and laboratory, in order to keep the proportion of diagnostic errors to a minimum.

POSTMENOPAUSAL UTERINE BLEEDING

To the Editor:—**Is the estrogenic component of various liver extract preparations potent enough to cause endometrial changes? A woman aged 70 began to bleed approximately twenty years after the menopause. She has been taking liver parenterally for several years. Curettage, carefully done, shows no malignant change. The pathologist reports "cystic hyperplasia." Pelvic examination reveals essentially normal conditions.**

M.D., Philadelphia.

ANSWER.—There is no appreciable estrogenic activity in liver extracts made for commercial purposes. It is difficult, therefore, to explain why this woman has uterine bleeding at the age of 70 except by placing the blame on the endogenous estrogens elaborated by the adrenal cortex. A number of authors have been able to detect an appreciable amount of estrogen in the body fluids of menopausal or castrate women; likewise, others have been able to obtain an occasional biopsy of the endometrium in menopausal women with cystic hyperplasia. It is conceivable that small amounts of estrogen elaborated for a period of years unopposed by the other elements of the normally secreting ovary such as progesterone might result in a bleeding episode. Nevertheless, the presence of the rare granulosa or theca cell tumor of the ovary must be ruled out in this case.

DETECTION OF PENICILLIN IN TREATMENT

To the Editor:—**Please give information regarding the best and most sensitive test now available for detection of penicillin in blood serum.**

M.D., Rhode Island.

ANSWER.—The determination of penicillin in blood serum depends on the serial dilution of serum to which an organism of known, high sensitivity to penicillin is added and compared with dilutions of a standard solution of penicillin prepared in a similar manner. A number of satisfactory methods have been described. The two most widely used are that of C. H. Rammelkamp (A Method for Determining the Concentration of Penicillin in Body Fluids and Exudates., *Proc. Soc. Exper. Biol. & Med.* **51**:95, 1942) employing a beta hemolytic streptococcus as the test bacteria and that of Randall and associates (Randall, W. A.; Price, C. W., and Welch, H.: Estimation of Penicillin in Body Fluids, *Science* **101**:365, 1945) employing Bacillus subtilis.

GOAT'S MILK

To the Editor:—**What are the main therapeutic considerations of goat's milk as against cow's milk? Is there any particular demand by internists or pediatricians for fresh goat's milk, and would there be much of a demand if the milk could be obtained canned—not in a condensed state? Is there any canning process available now (except the condensing process) which is satisfactory as regards keeping qualities, bacterial count and public health requirements? I am interested in the probable demand if the milk of the goat could be canned, evaporated and distributed.**

Bennett W. Muir, M.D., Denver, Colo.

ANSWER.—Both cow's milk and goat's milk are favorably regarded as human foods because they contribute essential nutrients. Comparative composition tables show some differences chiefly quantitative, in individual components.

A large number of therapeutic claims have been made for goat's milk, but available confirmatory evidence is meager Common practice is the use of goat's milk by persons who cannot tolerate cow's milk because of allergies or other reasons.

There is apparently no great demand for fresh goat's milk as evidenced by the small size of the goat milk industry in this country. Goat's milk is produced in appreciable quantities only in a few limited areas in the United States, one of which is in Colorado. It can be satisfactorily processed in tin either with or without removal of some of the water by evaporation. With the addition of vitamin D evaporated goat's milk is eligible for acceptance by the Council on Foods and Nutrition of the American Medical Association.

BLEEDING PEPTIC ULCER

To the Editor:—**What is the information on stopping bleeding peptic ulcers through the use of fibrin or other coagulants taken orally?**

M.D., Georgia.

ANSWER.—The use of coagulants taken orally for bleeding peptic ulcers has not been considered feasible because the agents are either inhibited or destroyed in the stomach. However, Daly reported (Use of Buffer Thrombin in the Treatment of Gastric Hemorrhage, *Arch. Surg.* **55**:208, 1947) that when 30 cc. of seventh-molar phosphate buffer, p_H 7.6, is given in order to neutralize and buffer the gastric contents and followed in five minutes by another 30 cc. of the buffer containing 10,000 units of thrombin, the action of the enzyme is preserved for a sufficient length of time to clot fibrinogen. In his preliminary report he concluded that thrombin given in such a manner is an aid in some cases in the control of gastric hemorrhage. No toxic effects have been observed. The author pointed out that heavy arterial bleeding and bleeding which ordinarily requires a ligature cannot be controlled by this substance alone.

REACTION: TETANUS ANTITOXIN

To the Editor:—Administration of tetanus antitoxin in small doses for passive protection without a preceding skin test is universally condemned but freely practiced. Should a skin test be performed? Is there danger of anaphylactic reaction without it? Could reaction follow the skin test alone? Would administration of diphenhydramine ("benadryl") or a similar drug confer protection?

M.D., Iowa.

ANSWER.—There is always danger that tetanus antitoxin may cause severe reactions in susceptible persons even if given in small doses for preventive purposes. Preliminary skin tests should be made to determine susceptibility to the antitoxin so that antitoxin can be given safely. Properly made skin tests do not cause general reaction. Whether drugs can be relied on to prevent anaphylactic reaction to tetanus antitoxin is not known.

URINARY INCONTINENCE

To the Editor:—An apparently healthly patient, aged 68, underwent a one stage suprapubic prostatectomy eleven weeks ago. No difficulties were encountered in enucleating the hypertrophied gland, and there was little bleeding. The prostatic bed was filled with four small strips of "oxycel" (absorbable oxidized cellulose), and a size 24 Foley catheter was introduced through the urethra, inflated to 30 cc. and withdrawn into the prostatic bed. Traction was not applied but the catheter was left loose. Ten hours later, as there was no active bleeding, the bulb was deflated and after another fourteen hours the catheter was entirely removed. Convalescence was uneventful. The suprapubic wound healed in ten days. The patient was discharged on the sixteenth postoperative day.

On his first office visit he complained of dribbling in the daytime. During the night he would wake up once or twice feeling the urge to urinate and then without getting out of bed he could void normally at will in the urinal. But as soon as he got up in the morning he would have to wear a pad constantly, and when he was working he kept on dribbling. He is discouraged and I am at a loss to promise much improvement. Is there any hope that he may become fully continent again? Should he keep on wearing a Cunningham clamp or should he wear a rubber urinal? Are there any treatments I could give him?

M.D., New Jersey.

ANSWER.—A slight degree of incontinence resulting from injury to the external sphincter is observed occasionally following removal of the prostate gland by any of the varjous surgical procedures employed. In most cases urinary control is recovered gradually in the course of time. The improvement may be slow, however, and eleven weeks after operation is too short a time to lose hope. Patients with postoperative incontinence have been observed in whom natural processes have corrected the condition as long as a year after operation.

If this patient is still incontinent after several additional months, it would be well for him to have a urethroscopic examination to see whether any actual sphincteric damage has occurred. It sometimes happens that a persisting nodule of prostatic tissue has fallen into the sphincteric area, which acts as a wick, preventing proper closure of the sphincter.

Meanwhile a Cunningham clamp is better than a urinal, but the patient should be encouraged to wear it only when absolutely necessary, while at work. While he is at home an athletic support and pads holding the penis up over the symphysis offer a much better method of caring for the incontinence.

Fortunately, permanent incontinence is seldom observed. In such cases surgical procedures to restore sphincteric action have not proved uniformly successful and should be considered only as a last resort. An artificial sphincter, such as that recently suggested by Foley, might be considered at some future date. Optimism and encouragement are the remedies that your patient needs at the present time.

VISUAL TESTS

To the Editor:—What are the equivalent values of visual acuity findings in the two methods of examining eyes wherein one uses 20 for the numerator in the different steps or amounts of visual acuity while the other uses 20 for the denominator? What are the different methods of eye examinations used to make determinations in both of the methods? What is the method of conversion used to obtain the equivalents?

Joseph Bogan, M.D., Arlington, Va.

ANSWER.—The English system uses feet and inches in recording visual acuity, the Continental uses the metric and the International (1905) uses the decimal system.

The record in one system is generally, though not invariably, transcribable into either of the other systems. In all three systems what is really the numerator of a fraction represents the relative distances from which the test object is viewed by the patient and the denominator represents the distance at which the normal eye should see this same test object. Thus 20/200 in the English system means that the patient is 20 feet away from a test object which he should see at 200 feet; in the Continental (metric) system this is 6/60, i. e. the patient is 6 meters from an object which he should see at 60 meters, and in the decimal system this is recorded as 0.1. Similarly $20/40 = 6/12 = 0.5$, and $20/20 = 6/6 = 10$ in the respective systems.

URINARY BALANTIDIASIS

To the Editor:—We have found Balantidium coli in the urine specimens of 3 patients. Two of these patients had diffuse aches and pains, weakness, anorexia, and loss of weight. They had had a mild febrile reaction. We have been unable to establish the pathogenicity of this parasite. Please send information, and give an opinion as to the pathogenicity of this organism? I might add that Dr. G. A. Slusser found some in a specimen of urine obtained during a ureteral catherization.

S. M. Ramer, M.D., Silver City, N. Mex.

ANSWER.—The normal habitat of Balantidium coli is the pig, monkey and man. Man becomes infested by ingestion of cysts of the organism. Though the organism conceivably may be transferred directly from man to man, some 25 per cent of cases of balantidiasis can be traced to direct contact with pigs. Since the disease is rare, although exposure in stockmen and in the abbatoir is high, it follows that in general the pathogenicity of this ciliate is of a low order. Experimental transference of the disease from pig or monkey to man has been unsuccessful.

After excystation in the small bowel, the highly motile trophozoites invade the submucosa of the large bowel, producing ulcerations resembling those of Endameba histolytica. Small mucoid abscesses containing the parasites are formed, surrounded by round cell infiltration.

Symptoms usually are those of chronic dysentery, varying widely in severity. Colic, bloody diarrhea, malaise and weight loss have been described. Prognosis is usually good except in persons debilitated by other disease or by senility, in whom mortality may vary from 5 to 30 per cent.

The presence of B. coli in the urinary tract is considered a great rarity, and authentic reports are scanty. Pathogenicity in this site seems to be nil, unless accompanied by other infection, in which event B. coli is believed to be merely an aggravating factor. The alkaline medium of the bowel is more favorable to the growth of the organism than the usually acid urine.

The route by which B. coli gains access to the urinary tract is open to some question. The organisms are known to invade lymph channels, lymph nodes and capillaries, thereby making systemic involvement possible. In cases which have been reported, however, it seems probable that retrograde infestation took place. The case of a homosexual Moroccan, exhibiting gross hematuria and discreet ulcerations of the bladder, proved to have a mixed infection of bilharziasis (schistosomiasis) and balantidiasis of the urinary bladder (Remlinger, P.; Cabane, G., and Bailly, J.: Infection vésicale mixte à "Bilharzia haematobia" et à "Balantidium coli," *Presse méd.* **46**:1730-1731 [Nov. 23] 1938). There was no evidence of B. coli in the bowel.

It would be of considerable interest and value to elicit a history of contact, and to ascertain whether or not the colon was also involved in the cases described. In the absence of concomitant colonic infestation it is unlikely that B. coli is responsible for the symptoms.

FECAL FISTULA FOLLOWING APPENDECTOMY

To the Editor:—In *The Journal*, April 19, 1947, p. 1254, Dr. Thomas W. Kredel, Indiana, Pa., asks about fecal fistula following appendectomy.

The reply does not mention a common cause of postappendectomy fecal fistula, namely regional ileitis, which in the acute attack can simulate acute appendicitis. If the terminal ileum is not carefully examined or the disease is not recognized, a normal appearing appendix is usually mistakenly removed.

Unquestionably this disease sooner or later involves the cecum, and removal of the appendix seems to hasten or make worse already existing inflammatory changes in the c um with resulting blow out of the appendical stump. A silk purse string suture has less chance of being followed by fistula than would a simple ligation of the stump but is no guarantee against this serious complication.

Regional enteritis has a well known symptomatology, and in the acute stage surgical intervention is not indicated.

R. M. Cunningham, M.D., Baltimore.

SENILE OSTEOPOROSIS

To the Editor:—In *The Journal* of Dec. 13, 1947, Queries and Minor Notes, two queries concerned osteoporosis of the spine. One (p. 1041) was entitled "Periodic Spasm of the Lumbar Muscles" (C. W. Atherton, M.D., Fairview, Ill), and the other (p. 1042) was entitled "Senile Osteoporosis" (M.D., California). Since both articles seem to be in the same vein, I should like to make a suggestion which was not offered in the replies. Dr. Fuller Albright, Boston, has brought out quite definitely the relationship of the endocrine system to the osteoporosis which occurs particularly in women over the age of 40 or which may occur following the cessation of menstruation. It is due specifically to the failure of formation of the protein bone matrix; consequently, calcium salts cannot be deposited as they are in the normal person. It is not necessarily due to a lack of calcium. In fact, the addition of calcium to the diet, together with vitamin D, may actually be harmful. Suggested treatment for this type of osteoporosis might be the use of androgens in doses of 25 mg. three times weekly together with estrogenic substance, about 6,000 units five times weekly or diethylstilbestrol 2 to 5 mg. per day. An adequate diet containing sufficient minerals, vitamins and calcium should be provided; however, it is hardly ever necessary to add additional calcium to the diet.

C. A. Splithoff, M.D., Oakland, Calif.

JOURNALS ABSTRACTED IN THE CURRENT MEDICAL LITERATURE DEPARTMENT, JANUARY—APRIL 1948

Titles have been listed or abstracts made of important articles in the following journals in the Current Literature Department of THE JOURNAL during the past four months. Any of the journals, except those starred, will be lent by THE JOURNAL to subscribers in continental United States and Canada and to members of the American Medical Association for a period not exceeding three days. Three journals may be borrowed at a time. No journals are available prior to 1937. Requests for periodicals should be addressed to the Library of the American Medical Association and should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Thus most of these journals are accessible to the general practitioner.

Acta chirurgica Scandinavica. Stockholm.
Acta clinica belgica. Brussels.
Acta medica orientalia. Jerusalem.
Acta medica scandinavica. Stockholm.
Acta obstetricia et gynecologica Scandinavica. Stockholm.
Acta orthopaedica Scandinavica. Copenhagen.
Acta psychiatrica et neurologica. Copenhagen.
Acta radiologica. Stockholm.
American Heart Journal. St. Louis.
American Journal of Clinical Pathology. Baltimore.
American Journal of Digestive Diseases. Fort Wayne, Ind.
*American Journal of Diseases of Children. A. M. A., Chicago.
American Journal of Hygiene. Baltimore.
American Journal of the Medical Sciences. Philadelphia.
American Journal of Medicine. New York.
American Journal of Obstetrics and Gynecology. St. Louis.
American Journal of Ophthalmology. Cincinnati.
American Journal of Pathology. Ann Arbor, Mich.
American Journal of Physiology. Baltimore.
American Journal of Public Health. New York.
American Journal of Roentgenol. and Radium Therapy. Springfield, Ill.
American Journal of Surgery. New York.
American Journal of Syphilis, Gonor. and Venereal Diseases. St. Louis.
American Journal of Tropical Medicine. Baltimore.
American Practitioner. Philadelphia.
American Review of Soviet Medicine. New York.
American Review of Tuberculosis. New York.
Anesthesiology. New York.
Annales medicinae internae Fenniae. Helsinki.
Annals of Allergy. Minneapolis.
Annals of Internal Medicine. Lancaster, Pa.
Annals of Otology, Rhinology and Laryngology. St. Louis.
Annals of the Rheumatic Diseases. London.
Annals of Surgery. Philadelphia.
Annals of Tropical Medicine. Liverpool.
Annals of Western Medicine and Surgery. Los Angeles.
*Archives of Dermatology and Syphilology. A. M. A., Chicago.
Archives of Diseases in Childhood. London.
*Archives of Internal Medicine. A. M. A., Chicago.
Archiv für Kinderheilkunde. Stuttgart.
Archivio italiano di chirurgia. Bologna.
*Archives of Neurology and Psychiatry. A. M. A., Chicago.
*Archives of Ophthalmology. A. M. A., Chicago.
*Archives of Otolaryngology. A. M. A., Chicago.
*Archives of Pathology. A. M. A., Chicago.
Archives of Physical Medicine. Chicago.
*Archives of Surgery. A. M. A., Chicago.
Archivos argentinos de pediatría. Buenos Aires.
Archivos de clínica. Rio de Janeiro.
Arizona Medicine. Phoenix.
Australian and New Zealand Journal of Surgery. Sydney.
Boletín de la Asociación médica de Puerto Rico. San Juan.
Blood. New York.
Brain. London.
British Journal of Dermatology and Syphilis. London.
British Journal of Experimental Pathology. London.
British Journal of Industrial Medicine. London.
British Journal of Ophthalmology. London.
British Journal of Radiology. London.
British Journal of Surgery. Bristol.
British Journal of Tuberculosis. London.
British Journal of Urology. London.
British Medical Journal. London.
Bruxelles-médical. Brussels.
Bulletin of the Johns Hopkins Hospital. Baltimore.
Bulletin of the New York Academy of Medicine. New York.
Bulletin of the U. S. Army Medical Department. Washington, D. C.
California Medicine. San Francisco.
Canadian Medical Association Journal. Montreal.
Cancer Research. Baltimore.
Cardiologia. Basel.
Cervello. Naples.
Chirurg. Würzburg.
Cincinnati Journal of Medicine. Cincinnati.
Connecticut State Medical Journal. Hartford.
Delaware State Medical Journal. Wilmington.
Deutsche medizinische Wochenschrift. Stuttgart.
Diseases of Chest. Chicago.

*Cannot be lent.

Edinburgh Medical Journal.
Endrocrinology. Springfield, Ill.
Experimental Medicine and Surgery. Brooklyn.
Gastroenterology. Baltimore.
Geriatrics. Minneapolis.
Giornale di clinica medica. Parma.
Giornale di medicina. Palermo.
Glasgow Medical Journal.
Gynaecologia. Basel.
Hawaii Medical Journal. Honolulu.
Illinois Medical Journal. Chicago.
Indian Medical Gazette. Calcutta.
Industrial Medicine. Chicago.
Irish Journal of Medical Science. Dublin.
Journal of Allergy. St. Louis.
Journal of the Arkansas Medical Society. Fort Smith.
Journal of Aviation Medicine. St. Paul.
Journal of Bacteriology. Baltimore.
Journal of Bone and Joint Surgery. Boston.
Journal of Clinical Investigation. Boston.
Journal of Endocrinology. London.
Journal of Experimental Medicine. New York.
Journal of the Florida Medical Association. Jacksonville.
Journal of Gerontology. Springfield, Ill.
Journal of Hygiene. London.
Journal of Immunology. Baltimore.
Journal of the Indiana State Medical Association. Indianapolis.
Journal of Industrial Hygiene and Toxicology. Baltimore.
Journal of Infectious Diseases. Chicago.
Journal of International College of Surgeons. Chicago.
Journal of Investigative Dermatology. Baltimore.
Journal of the Iowa State Medical Society. Des Moines.
Journal of the Kansas Medical Society. Topeka.
Journal of Laboratory and Clinical Medicine. St. Louis.
Journal of Laryngology and Otology. London.
Journal of the Maine Medical Association. Portland.
Journal of the Medical Association of the State of Alabama. Montgomery.
Journal of the Medical Association of Georgia. Atlanta.
Journal of the Medical Society of New Jersey. Trenton.
Journal of Mental Science. London.
Journal of the Michigan State Medical Society. Lansing.
Journal of the Missouri State Medical Association. St. Louis.
Journal of the Mount Sinai Hospital. New York.
Journal National Malaria Society, Columbia, S. C.
Journal of Nervous and Mental Disease. New York.
Journal of Neurology, Neurosurgery and Psychiatry. London.
Journal of Neuropathology and Experimental Neurology. Baltimore.
Journal of Neurophysiology. Springfield, Ill.
Journal of Neurosurgery. Springfield, Ill.
Journal of Nutrition. Philadelphia.
Journal of Obstetrics and Gynaecology of the British Empire. Manchester.
Journal of the Oklahoma State Medical Association. Oklahoma City.
Journal of Pathology and Bacteriology. Edinburgh.
Journal of Pediatrics. St. Louis.
Journal of Pharmacology and Experimental Therapeutics. Baltimore.
Journal of the Philippine Medical Association. Manila.
Journal of Physiology. Cambridge.
Journal of the Royal Army Medical Corps. London.
Journal of the South Carolina Medical Association. Florence.
Journal of the Tennessee State Medical Association. Nashville.
Journal of Thoracic Surgery. St. Louis.
Journal of Tropical Medicine and Hygiene. London.
Journal of Urology. Baltimore
Journal-Lancet. Minneapolis.
Kentucky Medical Journal. Bowling Green.
Klinische Wochenschrift. Heidelberg.
Lancet. London.
Laryngoscope. St. Louis.
Maandschrift voor Kindergeneeskunde. Leyden.
Medical Annals of the District of Columbia. Washington.
Medical Journal of Australia. Sydney.
Medicine. Baltimore.
Military Surgeon. Washington, D. C.
Minnesota Medicine. St. Paul.
Nebraska State Medical Journal. Lincoln.
Nederlandsch Tijdschrift voor Geneeskunde. Amsterdam.
New England Journal of Medicine. Boston.
New Orleans Medical and Surgical Journal. New Orleans.

New York State Journal of Medicine. New York.
New Zealand Medical Journal. Wellington.
Nordisk medicin. Gothenburg.
North Carolina Medical Journal. Winston-Salem.
Northwest Medicine. Seattle.
*Occupational Medicine. A. M. A., Chicago.
Ohio State Medical Journal. Columbus.
Ophthalmologica. Basel.
Pediatría de las Américas. Mexico, D. F.
Pennsylvania Medical Journal. Harrisburg.
Physiological Reviews. Baltimore.
Plastic & Reconstructive Surgery. Baltimore.
Practitioner. London.
Praxis. Bern.
Prensa médica argentina. Buenos Aires.
Presse médicale. Paris.
Proceedings of Royal Society of Medicine. London.
Proceedings of the Society for Experimental Biology and Medicine. Utica, N. Y.
Progresso medico. Naples.
Psychosomatic Medicine. Baltimore.
Public Health Reports. Washington, D. C.
Puerto Rico Journal of Public Health and Tropical Medicine. San Juan.
Quarterly Journal of Medicine. Oxford.
Quarterly Journal of Studies on Alcohol. New Haven, Conn.
Radiology. Syracuse, N. Y.
Review of Gastroenterology. New York.
Revista de la Asociacion médica argentina. Buenos Aires.
Revista clínica española. Madrid.
Revista cubana de pediatría. Havana.
Revista española de tuberculosis. Madrid.
Revista médica de Chile. Santiago.
Revista médica de Rosario. Rosario.
Revista de psiquiatría y disciplinas conexas. Santiago.
Revista de urología. Caracas.
Revue belge de pathologie et de médicine expérimentale. Brussels.
Revue neurologique. Paris.
Rhode Island Medical Journal. Providence.
Rocky Mountain Medical Journal. Denver.
Sang. Paris.
Schweizerische medizinische Wochenschrift. Basel.
Semaine des hôpitaux de Paris. Paris.
Semana médica. Buenos Aires.
Southern Medical Journal. Birmingham, Ala.
Southern Surgeon. Atlanta, Ga.
Surgery, Gynecology and Obstetrics. Chicago.
Surgery. St. Louis.
Texas State Journal of Medicine. Fort Worth.
Thorax. London.
Transactions of the Royal Society of Tropical Medicine and Hygiene. London.
Tubercle. London.
Union Medicale du Canada. Montreal.
United States Naval Medical Bulletin. Washington, D. C.
Urologic and Cutaneous Review. West Palm Beach, Fla.
Virginia Medical Monthly. Richmond.
Western Journal of Surgery, Obstetrics and Gynecology. Portland, Ore.
West Virginia Medical Journal. Charleston.
Wiener klinische Wochenschrift. Vienna.
Wiener medizinische Wochenschrift. Vienna.
Wisconsin Medical Journal. Madison.
Yale Journal of Biology and Medicine. New Haven
Zeitschrift für Kinderheilknude. Heidelberg.
Zeitschrift für Vitamin-, Hormon- & Fermentforschung. Vienna.

SUBJECT INDEX

This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "OS," Organization Section; "ab," abstracts; the star (*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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Acad.—Academy
Am.—American
A.—Association
Coll.—College
Commn.—Commission
Comm.—Committee
Conf.—Conference
Cong.—Congress
Dist.—District
Div.—Division
Found.—Foundation
Hosp.—Hospital
Indust.—Industrial
Inst.—Institute
Internat.—International
M.—Medical
Med.—Medicine
Nat.—National
Pharm.—Pharmaceutical
Phys.—Physicians
Soc.—Society
Surg.—Surgery
Surgs.—Surgeons
S.—Surgical

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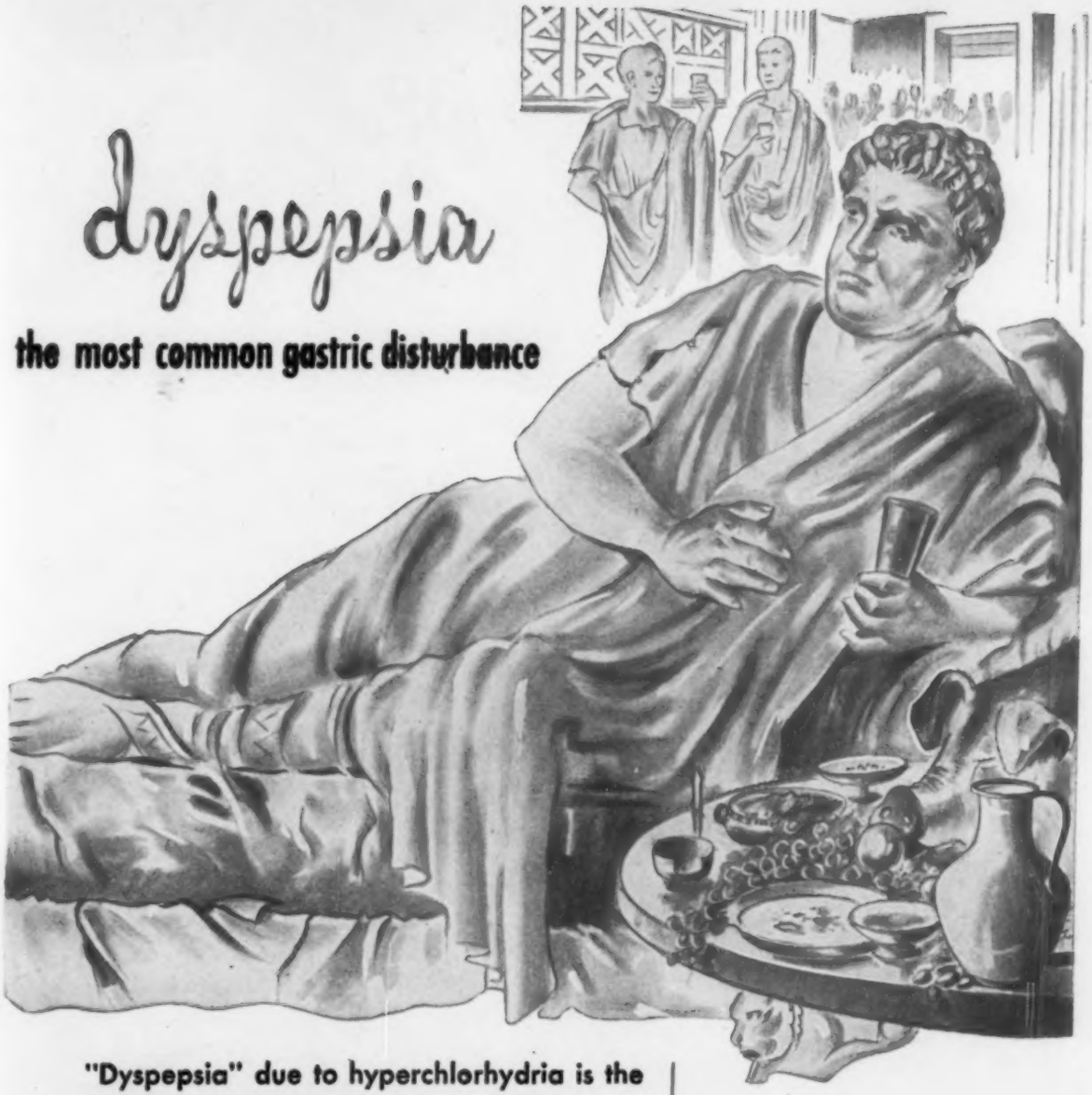
dyspepsia

the most common gastric disturbance



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